MEDICO-LEGAL ASPECTS OF BLOOD TYPE TESTING

A Dissertation submitted for the degree of Master of Laws of the University of Tasmania

by

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FOREWORD

In undertaking any work in the field known variously as that of forensic medicine, medical jurisprudence, legal medicine or medical law one suffers from the handicap of attempting to work simultaneously with two quite distinct disciplines: law and medicine. For some reason this field of study has been almost exclusively appropriated by the medical profession, and as lawyers know no medicine most of the works in this field, being written by the medical fraternity, are largely unintelligible to them. On the other hand doctors know little law, as any lawyer who has read textbooks of medical jurisprudence will testify, and one of the objects of this dissertation is to attempt to bridge this gap and redress the balance by providing an account of what is essentially a medical subject written by a lawyer (or, to avoid the language of exaggeration, one who is qualified as a lawyer) who is without any scientific training or experience. From the legal point of view, therefore, it is an exercise in "fact research"; an attempt to ascertain the factual basis underlying the practice of blood group testing.

There has been quite a flood of publications relating to blood groups in the last few years, but none have been primarily concerned with the medico-legal aspect of the problem. The only recently published works, known to us, which deal specifically with the medico-legal problems are Harley (1944) and Andresen (1952). Much has happened since these works were published, and we have here attempted to draw attention to all the major developments which had occurred up to the end of 1958.

In considering the purely legal problems that arise, absence of either English or Australian authorities has compelled us to refer to the relevant American authorities but we would emphasise that we have not attempted any account of the legal position in the United States. Such an analysis was beyond the resources available to us. Thus the American cases that have been cited are merely a selection of the large number that have been decided, selected simply on the basis of their usefulness as illustrative material.

No one can write on the subject of human blood groups without incurring a debt to the work of Race and Sanger, the third edition of whose book which became available to us whilst this dissertation was in course of preparation. It has never been far from our elbow; nor have the works of Mourant and Boorman and Dodd as will be obvious to all. A layman can obviously have nothing new to say on the subject of blood groups, but such is not our object. Our object is simply to present a sufficient background to the subject to make it intelligible to laymen, particularly to lawyers in the hope that with understanding both courts and practitioners will be more ready to make use of the technique of blood group testing.

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INTRODUCTION

BLOOD TRANSFUSION

It is a trite observation that there is nothing new under the sun, but it seems that the medico-legal applications of blood-group testing cannot be regarded as merely another of the applications of modern science for according to Furuhata (1949) the significance of mixing the blood of the parties in a paternity suit was well known to the Chinese as early as 1247 A.D. So far as Europe was concerned, however, this knowledge appears to have remained unknown for it is not until the nineteenth century that the iso-haemagglutination reaction is described in the literature.

The lateness of the recognition of this phenomenon is rather surprising in view of the fact that blood transfusions had been attempted since at least the seventeenth century, if not earlier, and many of the fatal accidents which resulted from these transfusions were undoubtedly due to haemagglutination.

The possibility of transfusion was actually suggested as early as the sixteenth century by Hieronymus Cardanus and Magnus Pegalius, whilst Andreas Libavius (1615) actually described a suitable technique, although it is uncertain whether he carried out the experiment that he described. Most modern work in this field dates, however, from the publication, in 1628 of Harvey's Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus. The first reported successful transfusions from one animal to another, usually ascribed to Francesco Folli, was carried out shortly after the publication of Harvey's work being performed in 1654. This was soon followed by further experiments, carried out in England by such persons as Sir Christopher Wren, Sir Robert Boyle Edmund King and Thomas Cox. In 1665 a second successful transfusion was carried out by Richard Lower in England who transfused the blood of one dog into another.

Credit for the first successful human transfusion (using sheep's blood) is usually accorded to Denys and Emmerez who performed the experiment at Montpellier in 1667, although in the same year J.D. Maior of Kiel also published an account of a human transfusion which may actually have preceded that of Denys and Emmerez. In the same year Richard Lower also succeeded in performing a successful human transfusion.

The way thus appeared to be open for substantial progress in this field when tragedy proved an obstacle which was to hinder any further advance for nearly a century and a half. One of Denys' patients died after a third transfusion in circumstances which, as Weiner (1946) has pointed out, strongly suggest that an haemolysis reaction had occurred. The patient's widow, however, claimed that Denys had poisoned her husband and although he was eventually acquitted the court decreed that no further transfusions were to be performed in France without the consent of the Faculty of Medicine in Paris, and in 1678 the Faculty prohibited all further transfusions after which nothing is heard of the technique until the nineteenth century.

Thus whilst, writing in 1667, Sprat could say that the transfusion experiements "will probably end in extraordinary success", Thompson, writing in 1812, said, "the expected advantages resulting from this practice have long been known to be visionary."

It was very shortly after Thompson thus wrote, however, that Blundell revived interest in the possibility of transfusion. His first paper was published in 1818 and in 1823 he published the results of an extensive series of experiments. This revival of interest was, however, short lived. Although in 1835 Bischoff described a method of using defibrinated blood, thus making it possible to avoid at least one of the major difficulties then experienced

in performing transfusions; that of coagulation, the continued persistence of fatalities inhibited development of the technique, and interest again waned.

A major step forward was taken in 1907 when Crile developed the technique of direct anastomosis, and in 1914 Hustin discovered the anti-coagulant properties of sodium citrate (the first transfusion using citrated blood being performed by Agote in the same year).[1] These developments coupled with the discovery of human blood groups by Landsteiner in 1900 rendered blood transfusio a relatively safe technique.

This brief sketch of the development of blood transfusion technique is not altogether irrelevant in an account of human blood-groups, for although the initial discovery of blood-groups was not made in connection with or as a result of blood transfusion, yet it is the practice of transfusion that has made possible much of the tremendous advance in human serology that has occurred in the last fifty years.[1]

DISCOVERY OF HUMAN BLOOD-GROUPS

The idea of specificity originated in the knowledge that, after recovery from an infectious disease, there remained an immunity from that particular disease - an idea which first found practical application in Jenner's vaccination against small-pox. It was the search for an explanation of this phenomenon that led to the discovery of anti-bodies. For a long time anti-bodies were only considered in relation to disease and it was only much later that it was recognised that immunisation against bacterial and toxic infection was merely one manifestation of a more general principle that applies whenever foreign substances are introduced into the serum. It was not until 1875 that Landois demonstrated species specificity when he showed that the blood of one species if introduced into another will cause the production of anti-bodies which will react with the foreign corpuscles by way of an agglutination reaction.

The fact that serological methods could be used to detect species differences naturally led to the question whether the same methods could detect individual differences within a species. It was in the investigation of this problem that the existence of human blood-groups was discovered. It was thus observed that if some types of human blood are mixed with other types of human blood an iso-agglutination reaction will occur. It was further found that this reaction was not a random reaction but followed very definite rules so that it was possible to classify human blood into a number of distinct categories according to the reactions they were capable of producing and undergoing.

By general consent priority in the description of this phenomenon is ascribed to Landsteiner who published his first paper on this subject in 1900. Unfortunately, however, there is a slight controversy over this point. Hamburger (1931) quotes observations by Creite dating back to 1869 whilst Kennedy refers to the

work of Maragliano which was published in 1892 and both suggest that priority may rest with these workers.[1] Neither of these claims, however, seems to be very seriously pressed. More strongly urged is a claim for priority on behalf of Shattock who published his observations in 1899. This claim is espoused by both Lattes (1932) and Kennedy. On the publication of Kennedy's article Zinsser and Coca (1931) sprang to Landsteiner's defence, although they themselves admitted: "it is not impossible that in some of his (Shattock's) tests the iso-agglutination phenomenon may have been involved." They differ from Kennedy, however, on the question as to whether there is evidence of this in Shattock's own paper.[3]

The point, however, is of little significance since even if, as Kennedy claims, Shattock did describe reactions which were in fact iso-agglutination reactions, he was concerned with a totally different problem and did not describe the reactions as examples of iso-haemagglutination, his main concern being with rouleaux formation particularly when associated with certain pathological states.

Arguments as to priority of scientific discovery are usually rather sterile, and if they have any meaning at all it can only be in terms of priority of understanding not merely priority of observation.[1] Many people had observed apples fall or kettle lids rise before Newton or Watt, but they can hardly claim priority on this score.

Whilst it seems rather pointless to deny that any one had observed an iso-agglutination reaction before Landsteiner, Landsteiner's own position is unaffected even if it is conceded that the reaction had been observed earlier, for it cannot be denied that he had priority of understanding. It is, however, worth noting that von Decastello and Sturli, pupils of Landsteiner, writing in

1902, open their paper on the subject by saying:

> "Landsteiner und Shattock (sic) haben zu gleicher Zeit unabhängig von einander darauf hingewiesen, dass dem Blutserum mancher Menschen die Fähigkeit innewohnt, die rothen Blutkörperchen anderer Personen zu verklumpen."

Landsteiner's original paper described three blood groups, but before long a fourth was added. By general consent the first description of the fourth group is credited to von Decastello and Sturli in their paper to which we have referred above. Again, however, there is a controversy over the question of priority. Kennedy has claimed that von Decastello and Sturli whilst confirming Landsteiner's original conclusions merely noted a number of exceptions which, according to Kennedy, they did not realise formed a group in addition to Landsteiner's original three. Kennedy claimed priority in the recognition of four groups for Jansky whose paper was published in 1907. However, Zinsser and Coca have rallied to the defence of von Decastello and Sturli claiming that Kennedy has misunderstood the German text of von Decastello and Sturli's paper.

Kennedy based his interpretation of von Decastello and Sturli's work on the following extract from their paper, saying:

> "The following quotation from the paper by v. Decastello and Sturli substantiates such an interpretation: 'Die 4 Ausnahmen von dieser Regel verhielten sich so, dass das Serum auf kein einziges Probeblut einwirkte, also gar kein Agglutinin enthielt, während die Erythrocyten von jedem anderer Serum agglutinirt wurden, also nicht wie bei den übrigen Personen, zumindestens gegen einen Serumtypus widerstandsfähig waren."

Zinsser and Coca, commenting on this passage say:

> "Decastello and Sturli desdribe the fourth group with accuracy, defining it as one in which the serum possessed no agglutinins for the cells of other groups, but in which the cells were agglutinated by all the other sera. They describe four such cases, 2.5 per cent of the total number of specimens examined. In disucssing them they used the word 'Ausnahmen' by which they designated these cases as 'exceptions' to the rule that all human blood contains isoagglutinins

> Neither their language nor the manner of their discussion justifies the assumption that they meant to indicate that these cases were abnormal 'exceptions' of a fixed three-group classification. Such an interpretation can only be based on an inaccurate comprehension of the German text of their paper."

Whilst it is indisputable that von Decastello and Sturli correctly indicated the nature of the specimens which they described by the word "Aushahmen" it is submitted that the language of their paper does give some credence to Kennedy's view that they regarded the specimens as "exceptions" to the three-fold classification described by Landsteiner. The passage in their paper immediately preceding that quoted by Kennedy seems to indicate that the "Regel" to which their four cases were "ausnahmen" was indeed a rule of three-fold classification. The passage runs as follows:

> "Sehen wir zumächst von den Plazenten und ganz jungen Kindern ab, deren Verhalten später eingehend zu besprechen ist, so ergab die Untersuchnung bei sämmtlichen 155 Personen im Alter von mehr als 6 Monaten, mit Ausnahme von 4 Fällen, das Vorhandensein von agglutinirenden Substanzen im Serum, sowie die strikte Sonderung in 3 Gruppen."

There are, however, other considerations which seem to support Kennedy's claim on behalf of Jansky which are independent of arguments over the meaning of terms in von Decastello and Sturli's paper.

In the first place there is nothing in the summary of Jansky's paper (written in French) which he appended to his original paper (which had been written in Serbian) which suggests that, as Zinsser and Coca claim, he was merely confirming the work of Decastello and Sturli.[1] It is perfectly true, as they point out, that his main concern was not to establish a classification of blood-groups.[1] It was rather, in his own words:

> "se servir practique ent des connaissance des hemolysines, des agglutinines, des precipitines, des toxines du sang et du serum chez alienes, sourtout chez les epileltiques et les paralytiques generaux."

His results, so far as this point was concerned, were negative, yet, summing up his results as a whole, he wrote as follows:

> "On peut resumer le resultat dans les regles suivants generalement valables:
> (1) Plusieurs serum humains se font remarquer par une puissance agglutinative identique a l'egard des globules rouges de certaines personnes et il est possible de les classer selon leur'efficacite en 4 groupes."

Jansky then goes on to define each of the four groups in terms of their power to agglutinate and undergo agglutination.

A second point which may be made is that if, as Zinsser and Coca claim, Kennedy misinterpreted the German text of von Decastello and Sturli's paper he was certainly not the only one to do so.[1] Writing in 1907 Hektoen stated:

> "Landsteiner and, following him, Decastello and Sturli point out that individuals may be separated into three main groups by means of iso-agglutination....."

and he adds that there are but "few exceptions" to this grouping. In 1908 Epstein and Ottenberg, in a paper in which they suggested that blood-groups were inherited, state:

> "It was first pointed out by Landsteiner, and later by Hektoen, Gay and others, that according to the mutual agglutinations of their séra, bloods could be divided into three classes."

Again in 1910 Moss published an account of his own work in which he also announced a four-group theory, but in a postscript noted that Jansky's paper had only come to his attention after the preparation of his own, and he added:

> "Had this paper come to my notice in time I could have given the author credit in the body of the paper for his priority in establishing the correct classification."

Finally we may note that in 1921 the American Immunological, Pathological and Bacteriological Societies officially recognised the priority of Jansky's work in recommending the use of his classification rather than that of Moss, and did so expressly "on the basis of priority". At that date, therefore, there were only two competitors for the standard classification. Landsteiner's original classification was simply A, B and C and no terminology appropriate to a four group classification appears to have been suggested prior to Jansky's work.

We can only conclude that if in fact von Decastello and Sturli did establish a fourth group this does not appear to have been generally appreciated at the time. Jansky certainly appears to have been the first writer explicitly to set out a four group classification, but owing to the inaccessability of his paper it was not until after 1910 that the four group classification was generally recognised.

We may end this section of our introduction by briefly noting the major advances that have been made in the subject since 1900-1902. The first major advance made after the establishment of the four-fold classification of the ABO system derives from the suggestion made by Epstein and Ottenberg in 1908 that blood groups might be inherited as Mendelian characteristics. In 1910 this suggestion was proved by von Dungern and Hirszfeld although it was not until 1924 that the correct genetic mechanism was discovered by the mathematicia Bernstein.

In 1911 von Dungern and Hirszfeld first described the existence of sub-groups within the ABO system and in 1918 Hirszfeld and Hirszfeld first reported the fact that the frequency of distribution of blood groups varied from

population to population; a fact which is the foundation of the use of blood-groups in anthropological work.

In 1927 Landsteiner and Levine added two new blood group systems: the MN and the P whose discovery was the result of testing human blood with animal sera, by which means antigens could be discovered for which there were no naturally occurring antibodies in human sera.

The next major step forward, and probably the most important since the original discovery of the ABO system, was the discovery of the Rh system by Landsteiner and Weiner in 1940. The discovery that the antibodies produced by the immunisation of rabbits and guinea pigs with the blood of the rhesus monkey agglutinated not only monkey red cells but also the blood of 85% of white people not only led to discovery of the Rh blood system but also uncovered the cause of the hitherto mysterious erythroblastosis foetalis thus making a notable contribution to clinical medicine as well as to serology.

Since 1940, and particularly in the post-war period progress has been fast and furious so that at the date of writing nine blood-group systems are known most of which are of considerable complexity, whilst in addition there are also numerous other blood factors which are either classified as "public" or "private" according to the frequency of their occurrence. Counting all these together the total number of theoretically possible blood types is raised to many millions so that the day does not appear far distant when in point of sober fact it will be possible to speak of the "individuality of the blood" as Lattes, in 1929, boldly entitled his book, and if the present rate of progress is maintained it may well be, as Landsteiner suggested in his Nobel lecture, that blood will become as distinctive as finger-prints.

THE NATURE OF THE ISO-AGGLUTINATION REACTION

The iso-agglutination reaction is, as we have already emphasised, merely a particular manifestation of the more general principle by virtue of which the body reacts to the presence of foreign substances. All reactions of this type involve antigen-antibody systems and we can best understand the nature of the iso-agglutination reaction by briefly discussing the nature of these systems of which blood-groups are but one example.

We must first define our terms and we may note the following definitions:

> "An antigen is any substance which, when introduced parenterally into an individual who himself lacks that substance, stimulates the production of an anti-body, and which, when mixed with the antibody, reacts specifically with it in some observable way."
>
> "An antibody is a substance which appears in the plasma or body fluids as a result of stimulation by an antigen and which will react specifically with that antigen in some observable way." (Boorman & Dodd 1957)

The following points should be noted in respect of these definitions. First, the reaction between an antigen and the corresponding antibody is "specific", i.e. as a general rule an antibody will only react with its corresponding antigen, and with no other. Occasionally this "rule" is broken and cross-reactions occur, but these may be disregarded in so far as one confines one's attention to blood group antigens and antibodies, since cross-reactions are almost unknown in this field. (See page 36.)

A second point needing emphasis is that, as a general rule an antibody cannot occur in the plasma of an individual who himself possesses the corresponding antigen. If it did then, by definition, a reaction would occur between the two, and in many cases the results would be fatal. This is, indeed, the situation which occurs in the case of the transfusion of incompatible blood or in cases of erythroblastosis foetalis the results of which illustrate the effect of a breach of this rule. In one case, however, there may be an

exception to the rule without harmful effects. This is the case where the antibody is of the type known as a cold auto-antibody. These antibodies are not active at 37°C and therefore cannot react with their corresponding antigen in vivo, even though the two are present together in the same individual.

In the definition of an antibody given above it was stated that antibodies are produced by stimulation by the corresponding antigen. To this rule there are, however, a number of exceptions in which antibodies are present in the plasma but for which no antigenic stimulus can be traced. These antibodies are known as natural antibodies, those produced by stimulation by the corresponding antigen being known as immune antibodies: the process of their formation being known as immunisation.

Finally note must be taken of the way in which antibodies react with their corresponding antigens. So far as blood-group serology is concerned there are three types of reaction to be considered; precipitation, haemolysis and agglutination.

Precipitation occurs where the antigens are soluble and where this is so the antigen may react with its corresponding antibody in such a way as to cause precipitation of the antigen-antibody complex. Where this reaction occurs the antigen is known as a precipitinogen and the antibody as a precipitin.

Where the antigen is cellular the reaction with the corresponding antibody may take the form of lysis, or destruction of the cells. This reaction differs from the other two in that it needs the presence of an additional factor before it can take place; the additional factor being known as complement. Where this reaction occurs the antigen is known as a lysinogen and the corresponding antibody as a lysin. If the reaction involves lysis of red cells it is known more specifically as haemolysis, the antigen as an haemolysinogen and the antibody as a haemolysin. Where the red cells are haemolysed haemolglobin is liberated

into the supernatant fluid which it stains. The degree of haemolysis that has occurred can be measured by comparing the colour of the stained supernatant fluid with that of a control.

Agglutination, known more specifically as haemagglutination when applied in the field of blood group serology, is the most important of the three reactions from the point of view of blood-group testing. Like haemolysis it can only occur where the antigens are of cellular origin. The reaction between the antigen and the antibody takes the form of causing the red cells to agglutinate or clump. Where this reaction is involved the antigen is known as an agglutinogen and the antibody as an agglutinin. The agglutinins are adsorbed by the red cells containing the agglutinogen whose presence stimulated their production. The red cells thus become sensitised and agglutinate or clump as a result.

It is possible, however, for cells to become sensitised without actually agglutinating. This is the case where the antibody is of the type known as "incomplete". One type of incomplete antibody is known as an agglutinoid. An agglutinoid can sensitise red cells suspended in saline, but such cells will only agglutinate if suspended in a medium of high molecular weight, such as bovine albumin. Another type of incomplete antibody, which will not agglutinate cells suspended in bovine albumin, are known as crypt-agglutinoids. Red cells sensitised by such antibodies can, however, be made to agglutinate when suspended in anti-human-globulin (A.H.G).

The distinction between complete and incomplete antibodies is well illustrated by the following schematic diagram:

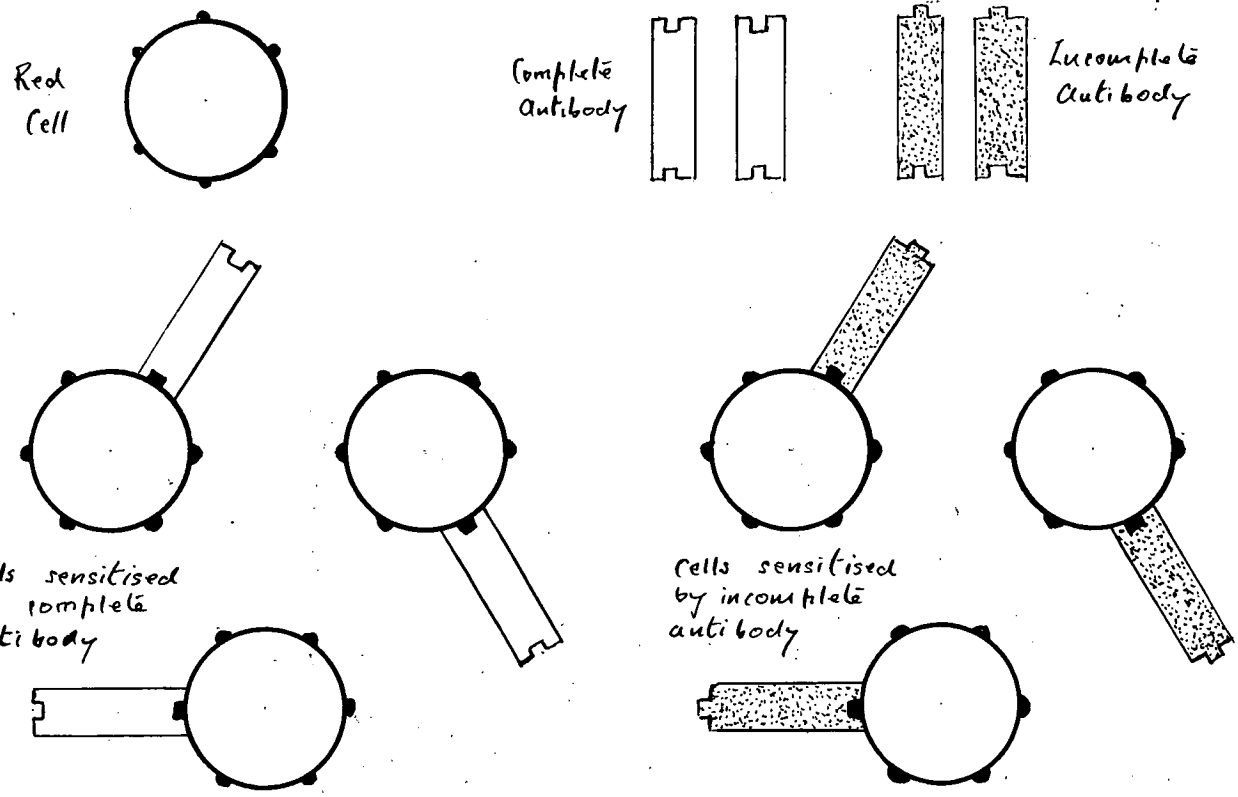
INHERITANCE OF BLOOD-GROUPS

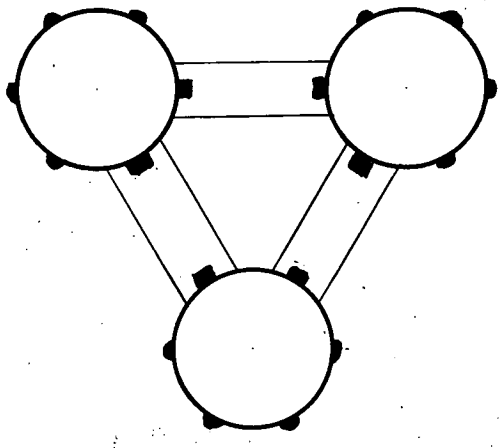
One of the most important medico-legal applications of blood-group testing, namely its application in disputed paternity proceedings, is based on the fact that blood-groups are inherited as Mendelian characteristics. The actual details of the inheritance of each of the blood-group systems will be discussed in due course, but as a background to such a discussion it will be helpful to sketch in a brief account of Mendelian genetics as the final part of our Introduction.

The story of the Abbé Mendel and his experiments with garden peas has often been told and need not be repeated here. It will be sufficient to set out the results of his experiments which he summed up in two laws.

The first law, known as the Law of Segregation, may be stated as follows: Inherited characteristics are controlled by a pair of genes the members of which segregate during game to genesis, passing into different gametes, pairs being restored in the zygote as a result of syngamy.

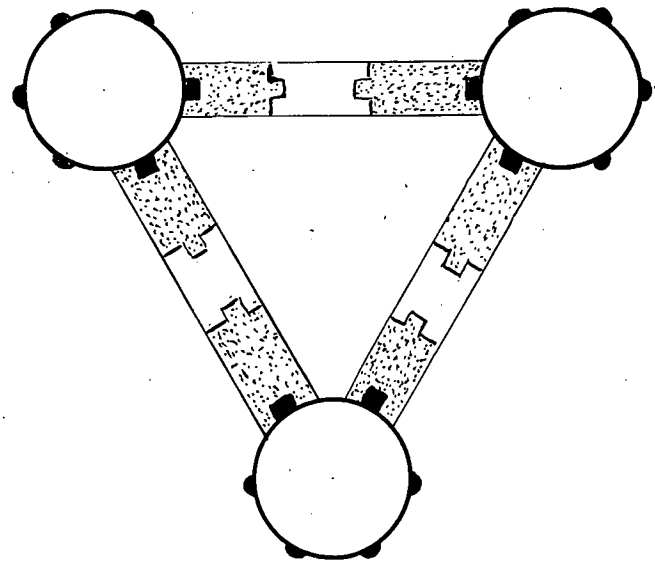
The genes referred to in Mendel's first law are carried on chromosomes which are thread-like structures found in the nuclei of the reproductive cells. These chromosomes occur in pairs, and in man there are now known to be 23 pairs (not 24 as formerly believed)./ (Ford and Hammerton, 1956) A given pair of genes, controlling one characteristic will be carried on a pair of chromosomes (one gene on each chromosome of the pair). The genes of a pair each occupies the same position or locus on their chromosome. There may be more than one kind of gene which ca occupy the same locus. Such alternative types of genss, which determine alternative characteristics are known as alleles, allelomorphs or allelic genes.





Cells agglutinated by complete antibodies

(Adapted from Dunsford & Bowley 1965)



Cells sensitised by incomplete antibodies, agglutinated by anti-human globulin serum.

To discuss the segregation of the genes during gametogenesis it is necessary very briefly to consider the method of human reproduction. Human reproduction is effected by means of the fusion of two cells known as gametes; that supplied by the male being a spermatazoon and that supplied by the female being an ovum. The gametes are derived from spermatocytes and oocytes respectively, the process of their formation being known as gametogenesis. The fusion of the gametes (syngamy) results in the formation of a zygote, a cell whose genetic constitution is derived from the chromosomes contributed by each of the gametes from whose fusion it results. The zygote, whose formation is the first stage in embryological development, carried the full human complement of chromosomes. It therefore follows that the gametes themselves cannot have carried the full human chromosome complement, for if they had done so the zygote would carry a double set of chromosomes.

In fact the gametes only carry half the full number of chromosomes (the haploid number) for in the process of their formation from the spermatocytes and oocytes respectively a meiotic or reduction division occurs such that the chromosome complement of the spermatocyte or oocyte is divided between two spermatozoa or ova (or more precisely between an ovum and a polar body). Thus instead of carrying 23 pairs of chromosomes each gamete only carries 23 single chromosomes. With fusion of two gametes the full human complement of 23 pairs is restored in the zygote, of which half is derived from the male parent and half from the female. It is the process of segregation during meiotic division which is referred to in Mendel's first law.

This process of segregation may be illustrated by taking a simple case. Consider the rather curious characteristic, the ability to taste a substance known as phenyl-thio-urea.[1] This characteristic is known to be inherited and to be controlled by a single pair of genes which may be designated T and t: T being responsible for the ability to taste the substance and t being responsible for the inability to do so.[1] Now two such genes may be arranged in pairs in three different ways: TT, Tt and tt, and the pair of genes possessed by any individual may be any one of these three combinations. Where both genes of the pair are the same the individual is said to be homozygous; where they are different he is said to be heterozygous.

It is obvious that if T is responsible for the ability to taste phenyl-thio-urea, then a person whose genes are TT will be a "taster", whereas t being responsible for the inability to taste, a person whose genes are tt will be a "non-taster". This raises the problem of the position of the heterozygote i.e. a person whose genes are Tt. Will he be a "taster" or not? To answer this question we must introduce another fundamental concept, that of dominance. Of a pair of genes one may be dominant over the other, in which case the other is said to be recessive. The gene which is dominant will produce its effect even where it only occurs in a "single dose" i.e.[1] in the heterozygote, whereas a recessive will only produce its effect in a double dose, i.e. in the homozygote. In the case of ability to taste phenyl-thio-urea T (the ability to taste) is dominant over t (the inability to taste) so that in this case the heterozygote (Tt) will be a taster.

It should perhaps be added that of the genes in a pair it is not necessary that one should be dominant over the other; they may be co-dominant in which case the heterozygote will posses some of the characteristics of each of the homozygotes.

This leads to a further point. Whereas the genes T and t can occur in three types of pairs, there are only two recognisable manifestations: individuals are either tasters or non-tasters. These distinct manifestations, known as phenotypes, are related to the various genetic combinations, known as genotypes, as follows:

TT)
) .....Tasters
Tt)

tt .....Non-tasters

With that general background we can now use the example of ability to taste phenyl-thio-urea to illustrate the process of segregation and re-combination of genes. Consider the case in which both parties to the union are heterozygous i.e. have a genetic constitution Tt. The processes of segregation and re-combination may then be illustrated as in Fig. 2.

In this case the ovum happened to carry the t chromosome and was fertilized by a spermatozoon which also carried the t chromosome, so that the resulting zygote would have a genetic constitution tt, i.e. would be a non-taster although both of its parents were tasters. An equally likely possibility, however, would have been that the ovum had been fertilized by a spermatozoon carrying the T gene in which case the resulting zygote would have been heterozygous Tt and thus possessed the same genetic constitution as that of both parents. Again the ovum could equally well have carried the T gene

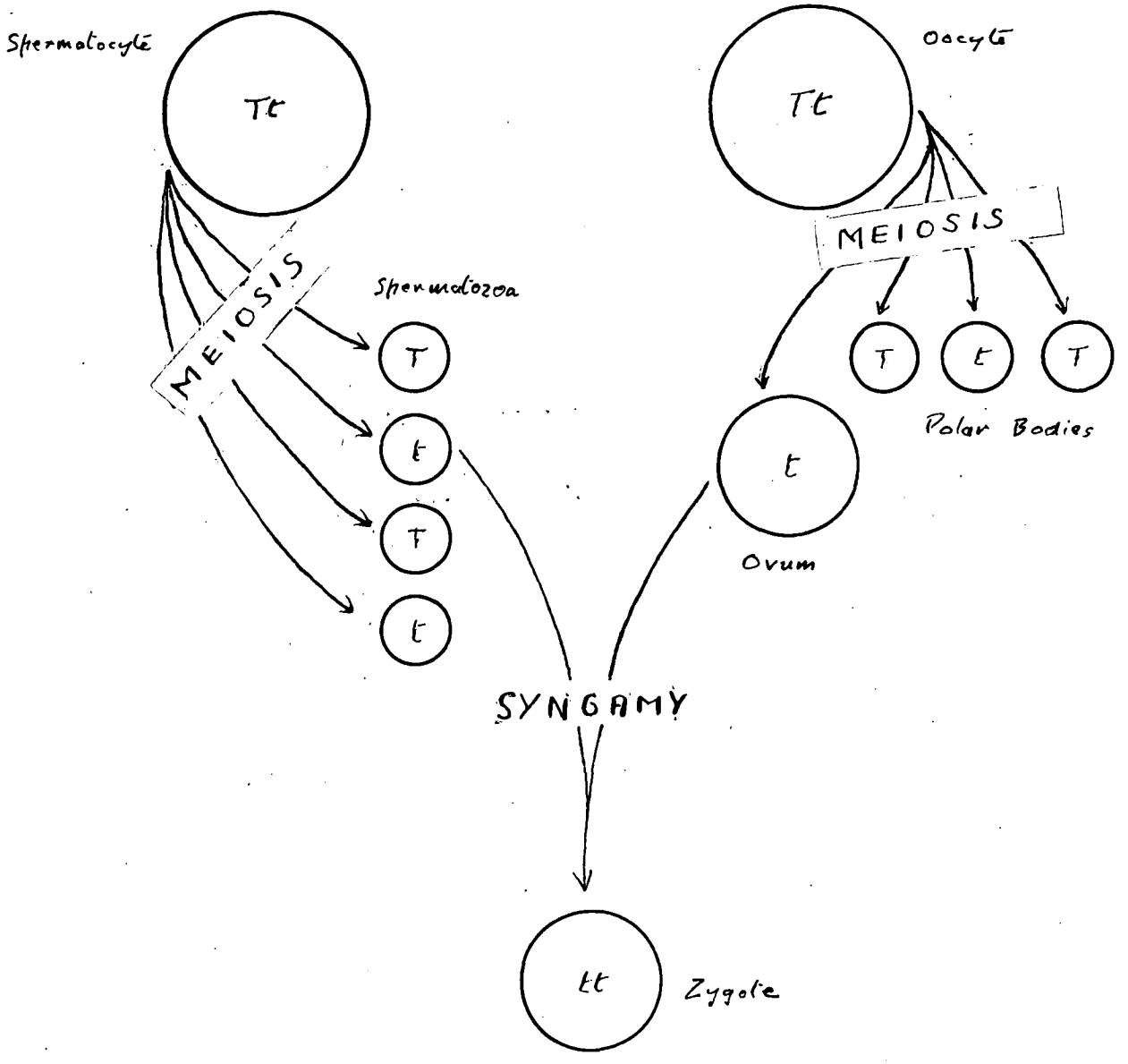

Spermatocyte
Tt
MEIOSIS
Spermatozoa
T
t
T
t
Oocyte
Tt
MEIOSIS
T
t
T
Polar Bodies
t
Ovum
SYNGAMY
tt
Zygote

Fig. 2.

in which case the zygote would have been TT or Tt according to the gene carried by the spermatozoon by which it was fertilized.

The various possibilities arising from such a situation may be shown diagrammatically in Fig. 3. It can be seen that where both parents are heterozygous the resulting offspring can have any of the possible genotypes and therefore be of any of the possible phenotypes. Where, however, both parents are homozygous and carry the same gene, or even where they are homozygous but carry different genes then the possibilities as to the genetic constitution of their offspring will be much more restricted as shown in Fig. 4.

Having thus briefly considered Mendel's law of Segregation we must turn to consider his second law, known as the Law of Independent Assortment, which may be formulated as follows: When two or more pairs of genes segregate the distribution of any one of them is independent of the distribution of the others. This law is now known to be only partially true, for as we have said above, the genes are carried on chromosomes and it is these latter which segregate during gametogenesis and not the genes themselves. (Since chromosomes had not been discovered at the time Mendel did his work he naturally thought in terms of the genes segregating independetly).

Genes which are carried on the same chromosomes are said to be "linked" for they will usually segregate together. The extent to which they will do so, however, depends upon how close they are together on the chromosome, for associated with the segregation of chromosomes during gametogenesis is the phenomenon of "crossing-over" as a result of which, before segregation, sections of each of two members of a pair of chromosomes change places. The closer that two genes are on a chromosome the less likely is it that they will become separated as a result of crossing-over. The effects of crossing-over may

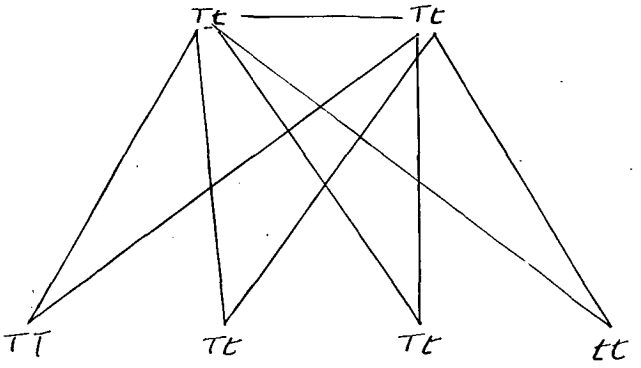
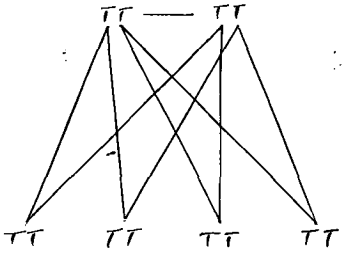


Fig. 3



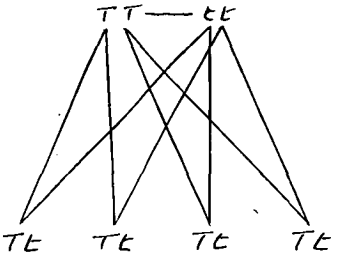


Fig. 4

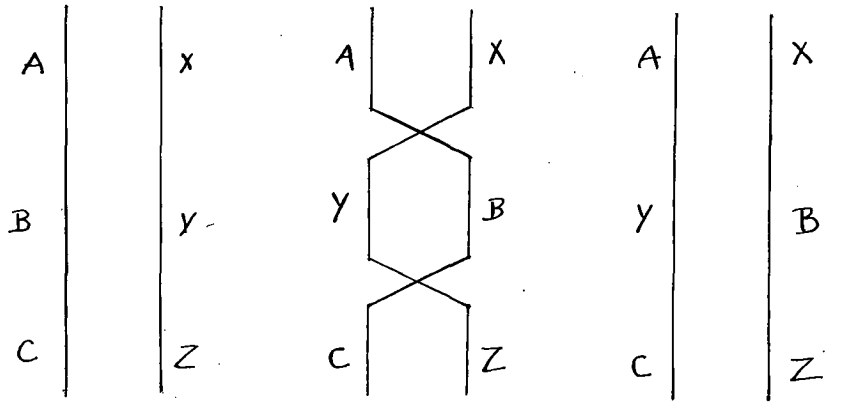


Fig. 5

crossing over showing the formation of two chiasmata

be illustrated diagrammatically as in Fig. 5.

The process of segregation when there are several chromosomes each carrying several genes is exactly the same as that discussed above in the case of a single gene, although diagrammatic representation becomes rather complex. It will be sufficient to illustrate by means of a case involving two pairs of chromosomes each carrying three pairs of allelomorphs as in Fig. 6. Fig. 7 illustrates the same situation from a slightly different point of view, that of setting out the various genetic possibilities of the offspring. Considering that there are 23 pairs of chromosomes each carrying probably some hundreds of genes the complexity of man's total genetic situation can be imagined.

There is one conclusion which follows from the preceding discussion which cannot be stressed too much, namely, that no child can, at least under normal circumstances, carry any gene which is not carried by either of its parents. Thus to revert to the case of ability to taste phenyl-thio-urea, if both parents are homozygous tasters the child could not possibly be either a heterozygous taste or a non-taster, for to be so would mean that the child would have to carry the t gene which was carried by neither of its parents. The only possible circumstan in which a child could carry such a gene would be the very rare circumstance in which a mutation occurred. A mutation may be defined as a change in a gene which occurs between one generation and another. Although it is possible that allelomorphs themselves have arisen as a result of mutation, mutation itself is a very rare event. According to Ford (1956) "A mutation rate of 1 in 50,000 individuals is exceptionally high and rarely exceeded."

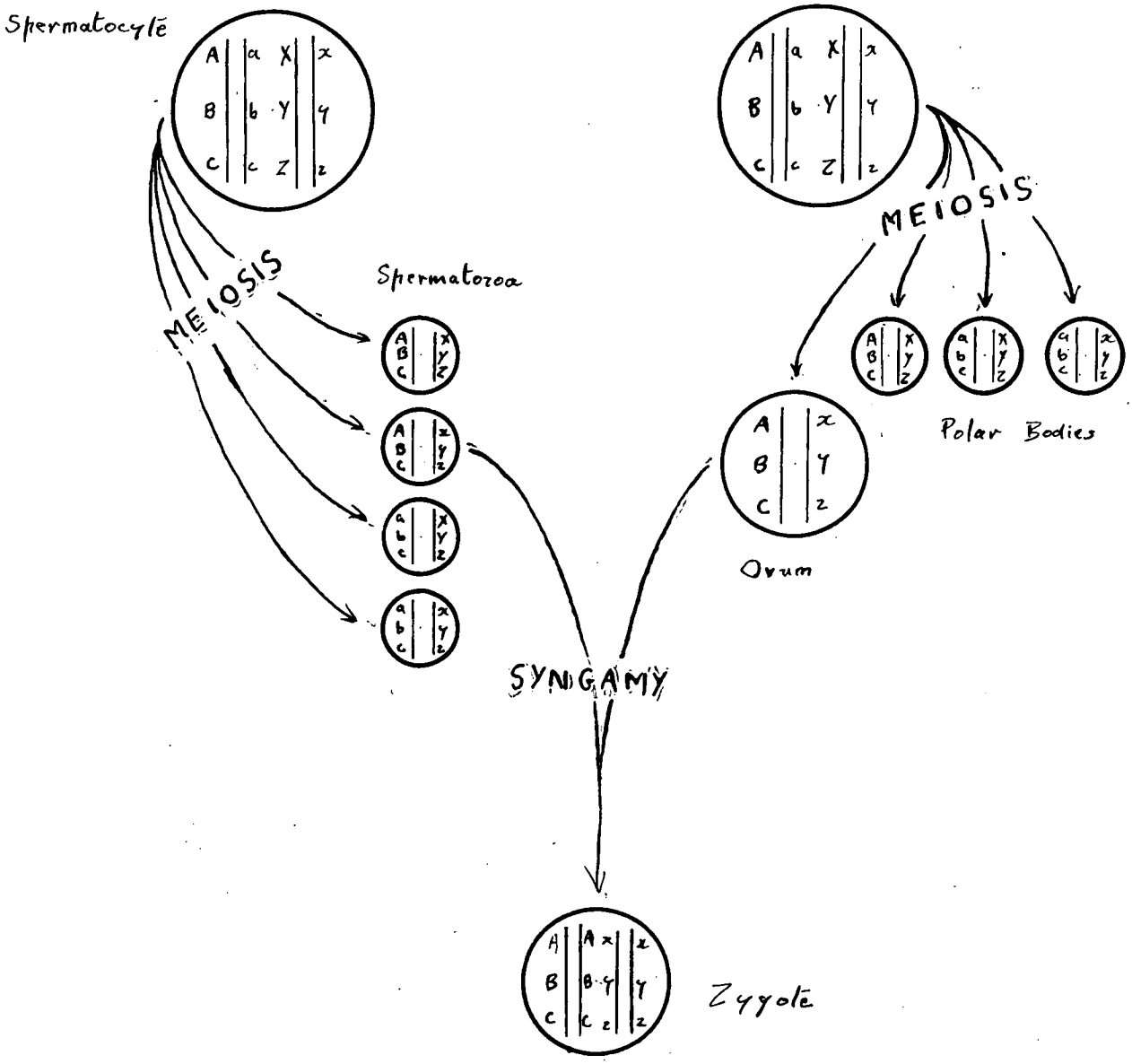
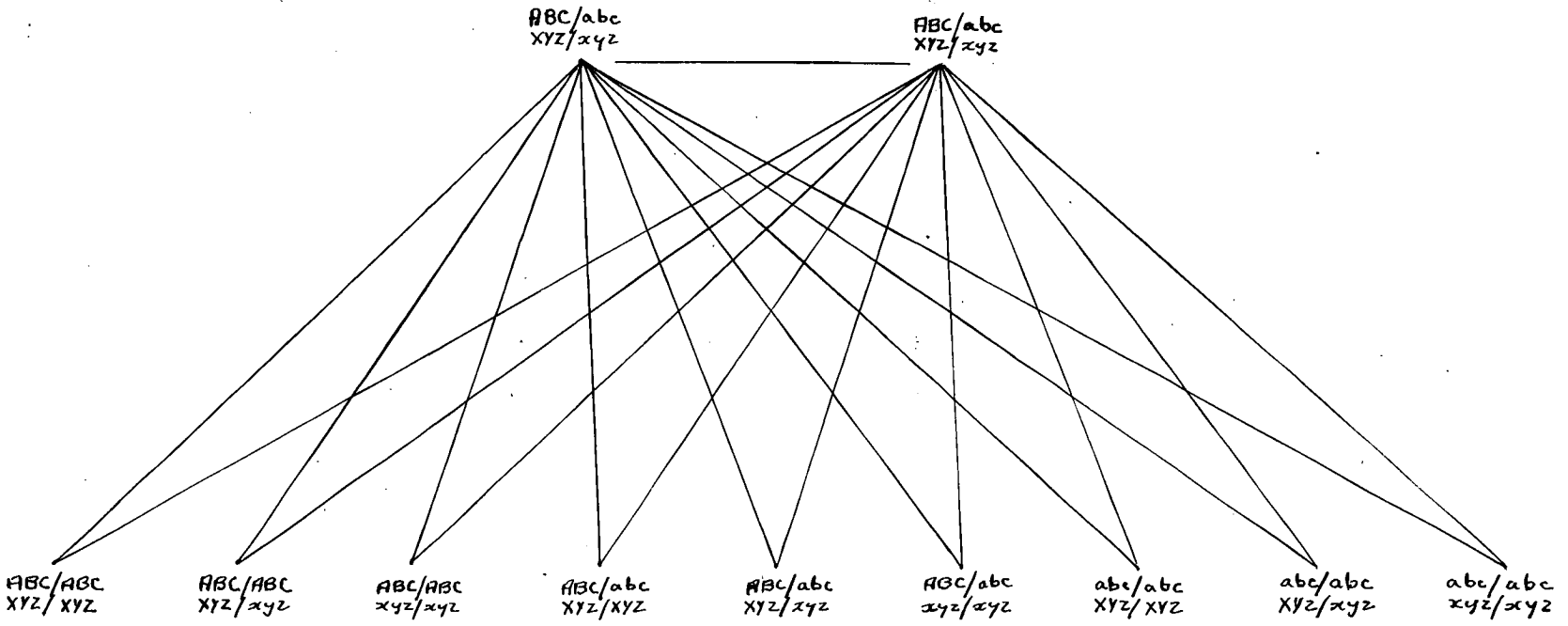

Spermatocyte
MEIOSIS
Spermatozoa
MEIOSIS
Polar Bodies
Ovum
SYNGAMY
Zygote

Fig. 6


ABC/abc
XYZ/xyz
ABC/abc
XYZ/xyz
ABC/ABC
XYZ/XYZ
ABC/ABC
XYz/xyz
ABC/ABC
xyz/xyz
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XYZ/XYZ
ABC/abc
XYz/xyz
ABC/abc
xyz/xyz
abc/abc
XYZ/XYZ
abc/abc
XYz/xyz
abc/abc
xyz/xyz

Fig. 7

THE ABO BLOOD-GROUP SYSTEM

The circumstances of the discovery of the ABO blood-group system have already been noted. The four blood groups initially discovered were explained on the basis of the reactions between two antigens and their corresponding antibodies. The terminology used to describe these is one which is traditional although no longer consistent with the nomenclature adopted in the case of the other blood-group systems. Thus the antigens are referred to as A and B, whilst the antibodies are designated α and β.

It is now generally agreed that three allelic genes are responsible for the basic ABO system, which are designated as A, B and R, of which R is recessive and A and B co-dominant. Now a system of triple allelomorphs can be arranged to give rise to six possible genotypes, whilst in the ABO system, as defined by the antibodies α and β, four phenotypes can be distinguished which are related to the six genotypes as follows:-

AA)
AR) .....A

BB)
BR) .....B

AB.....AB

RR.....O

The frequency of occurrence of the phenotypes in any given population can be obtained by simple testing and vast numbers of tests have been done on populations all over the world with ABO antibodies. (The results are all collated by Mourant, The ABO Blood Groups). The figures for the white population of Australia, summing the results of all the individual investigations

are as follows:-

Group	No.	%
O	122945	47.56
A	102735	39.75
B	25114	9.72
AB	7592	2.97
Total	258386	100.00

Sources: Tebbutt, 1922-23
Bryce et al, 1950-51
Walsh, 1947
Shipton, 1935-36
Kirk etal, 1953 and 1955
Kirk and Voss, 1957

One of the most outstanding features of blood group frequencies is the fact, discovered by Hirszfeld and Hirszfeld (1918) that distribution frequencies vary markedly from one population to another. This is strikingly illustrated if the distribution frequency for white Australians is compared with that for the aborigines. The figures for the latter are as follows:

Group	No.	%
O	1373	51.42
A	1217	45.56
B	71	2.66
AB	9	0.36
Total	2670	100.00

Sources: Phillips, 1927-28
Birdsell & Boyd, 1940
Tebbutt, 1922-23
Simmons et al, 1948
Lee, 1926
Cleland and Johnston, 1938
Gay, 1942

It should be noted that the figures for the aboriginal population show much greater variation than those for the white population. Thus individual investigators differed in the percentage frequency of the O gene by as much as 60% whilst the percentage figure for the A gene varied between 85.71 and 16.67. Despite these variations the outstanding feature of the aboriginal figures is the almost total absence of the B gene (even those few cases in which it was found are probably explicable on the basis of a recent introduction due to contact with other populations).

Using the phenotype frequency distribution figures the actual gene frequencies can be calculated. The methods used for these calculations will be discussed when the inheritance of the ABO system is considered. The results obtained, however, are as follows:

p 0.2446

q 0.0672

r 0.6882

where p represents the frequency of A, q the frequency of B and r that of O. It should be added that the above frequencies, based on the phenotype frequencies for the white population of Australia were calculated using Fisher's formulae.

The large number of published results relating to the distribution frequency of the ABO blood groups makes it possible to treat them statistically. Thus if all the published results for the British Isles be plotted on a graph a number of interesting conclusions become immediately apparent. On the following graph the results have been plotted with the frequency of the A

gene against that of the B gene, the axes being somewhat arbitrarily determined so as to include as many results as possible. It can clearly be seen that there is a marked distinction between the English and Irish figures particularly those relating to the distribution of the A gene. All the English results show a percentage frequency for the A gene greater than 20%, whereas all but a small number of the Irish results show a percentage frequency less than 20%. The Welsh results, whilst showing much greater variation than the others fall, in the main, within the range of the English figures. The Scottish results are too few for any conclusions to be drawn from their distribution.

The results plotted on the following graph were taken from Mourant (The ABO Blood Groups 1958) and include all the results for the British Isles with the exception of three English and two Welsh results. They were omitted simply because their inclusion would have necessitated the use of much smaller scales on the axes.

h

× = English figures
⊙ = Scottish figures
× = Welsh figures
× = Irish figures

13
14
15
16
17
18
19
21
22
23
24
25
26
27
28

q 4 5 6 7 9 10 11 12 q

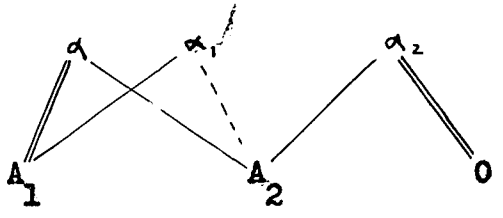
x h

SUB-GROUPS WITHIN THE ABO SYSTEM

The simplicity of the four-fold classification of human blood was destroyed as early as 1911 when von Dungern and Hirszfeld first demonstrated the existence of sub-groups. They found that if the serum of group B blood is absorbed with the cells of some group A individuals so that it is no longer capable of agglutinating those cells, the serum is still capable of agglutinating the cells of other group A individuals.

This discovery led to the recognition of the existence of two distinct antigens, A_1 and A_2 which increase the number of groups within the ABO system to six, namely, A_1, A_2, and A_1B, A_2B, B and O. The corresponding antibody system is not quite symmetrical, for associated with these antigens are two antibodies α and α_1, which react so that α agglutinates A_1 and A_2 whereas α_1, agglutinates the cells of only A_1.

A further antibody α_2 was at one time also described as belonging to this system, its relationship being that shown below



Source: Weiner after Friedenreich

It is now known, however, that α_2 is really an "anti-O" and will be discussed as such later.

Although the distinction between A_1 and A_2 was described as early as 1911, it was some time before it was recognised that distinct sub-groups

were involved. The delay was caused by doubt as to whether the difference between A_1 and A_2 was really qualitative; writers such as Lattes suggested that it was merely a quantitative difference. The qualitative nature of the distinction was, however, established as a result of the work of Lansteiner and Witt (1931) and Friedenreich and Zacho (1930). The former, by absorption and elution experiments, succeeded in separating the antibodies, whilst the latter, using absorbed B and sera were able to distinguish between A_1 and A_2 cells.

The relationship between phenotypes and genotypes in the ABO system as defined by , , and are as follows:

A_1A_1, A_1A_2, A_1O	A_1
A_2A_2, A_2O	A_2
A_1B	A_1B
A_2B	A_2B
BO, BB	B
OO	O

The frequency of distribution of the sub-groups can be established in the same way as those used in the case of the main groups. There seem to have been no tests made on the white Australian population using both anti-A and anti-A_1 but the relevant English figures will provide some guide.

They are as follows:

Group	No.	%
O	3639	43.02
A_1	2969	35.10
A_2	812	9.60
B	756	8.94
A_1B	221	2.06
A_2B	61	0.72
Total	8458	

Sources: Taylor and Prior, 1938
Ikin et al, 1939
Walther et al, 1956
Sanger and Race, 1949
Bertinshaw et al, 1950
Tovey, 1952
Simson - quoted by Weiner
Thomas and Hewitt - quoted by Weiner
Garlick and Pantin, 1957

From the phenotype distribution frequencies the gene frequencies can be calculated in the usual way. The results calculated by Stevens, using Fisher's maximum likelihood method based on the figures obtained by Ikin et al.(1939) are as follows:

r 0.660226

p_1 ..... 0.208959

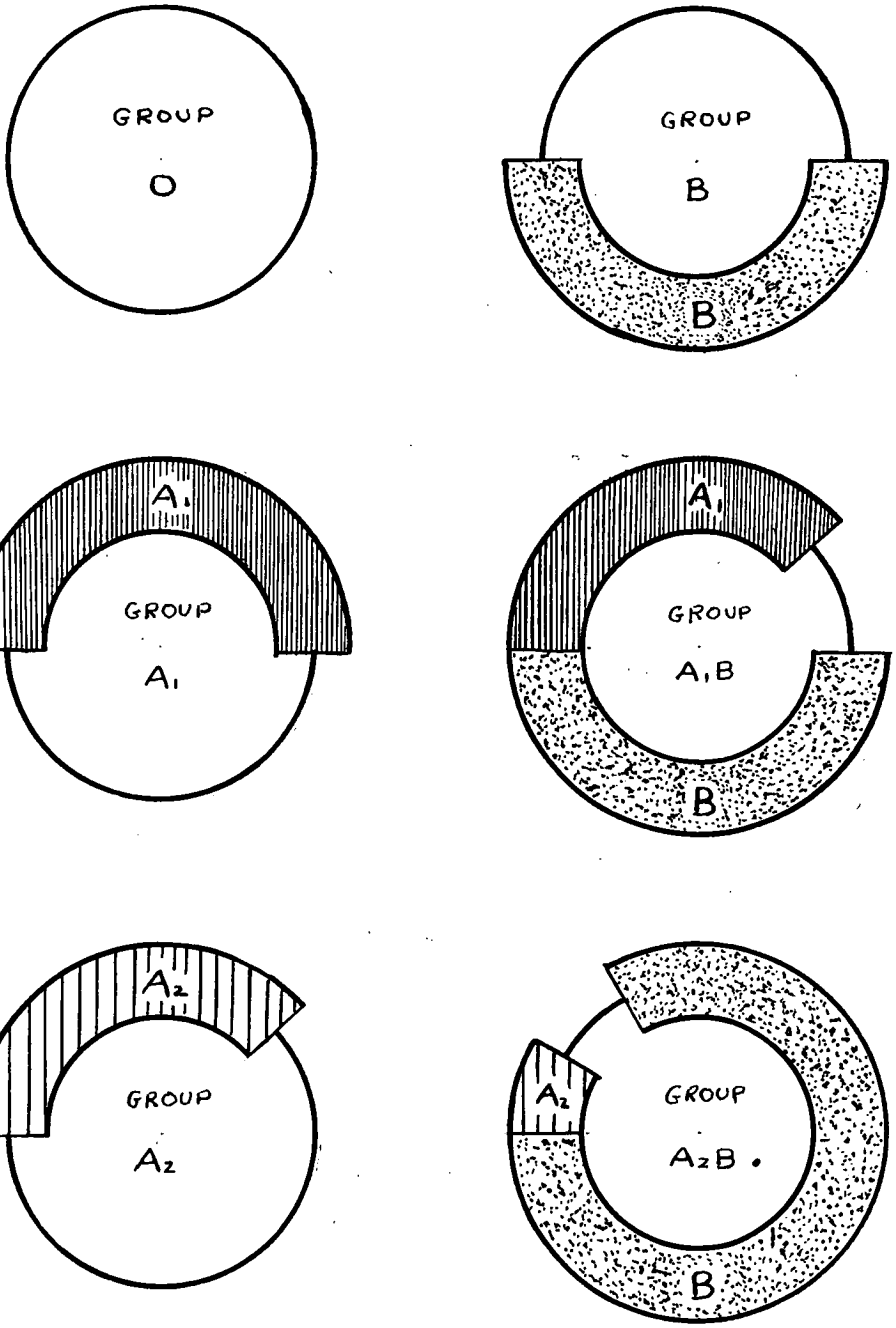
p_2 ..... 0.069649

q 0.061166

A point which should perhaps be emphasised is that the antibody , (also known as anti-A_1) can cause anomalous results in that it may occur as a typical cold auto-agglutinin in the sera of individuals of group A_2 and A_2B as well as a typical agglutinin in the sera of persons of group B and O.

As was implied in the gene frequency distribution figures given above, the existence of sub-groups within the ABO system is found to be dependent upon the existence of a fourth allelic gene. The four allele theory was put forward by Thomsen et al, (1930) as a modification of Bernstein's three allele theory (1924).

Hirszfeld's theory as to the antigenic composition of the red cells within the ABO system is shown by the diagram in Fig. 8.



Source Boyd (1937)

FURTHER DEVELOPMENTS IN THE ABO SYSTEM

Developments within the ABO system after the establishment of the sub-groups A_1 and A_2 have proceeded along two main lines. The first is associated with the discovery of still further "sub-groups" within the system, the antibodies concerned being extremely weakly reacting antibodies. The second main line of development has concerned the concept of group O. Although these two lines of development are related, it will be convenient to discuss first the additional sub-groups of the ABO system before going on to discuss the modern developments in the concept of group O.

Friedenreich (1936) described a weak entigen which he called A_3. This antigen is not only very weak but also very rare. Gammelgaard (1942) has estimated that it occurs no more than once in a thousand group A individuals. Although Cotterman (1956) has suggested that A_3 is a combination of A_2 and O, both Friedenreich and Gammelgaard consider that the gene responsible is an allele at the A_1A_2 locus.

In 1940 Gammelgaard and Marcussen described an even weaker antigen, known as A_4. Whether this is really a distinct sub-group or not does not appear very clearly from the literature. It is so described by Boorman and Dodd (1957), but not by Race and Sanger (1958).

Another possible sub-group within the ABO system is that reported by Fischer and Hahn (1935) the antigen of which is usually known as A_x. Not all the authorities are completely consistent on this point however. Race and Sanger (1958) imply that Fischer and Hahn's A_x is the same as Gammelgaard and Marcussen's A_4, whilst Weiner (1946) and Harley (1944) seem to consider that it is the same as Friedenreich's A_3. It is hardly possible, therefore, to

say very much here as to who is right. The difficulty in working with such very weak antigens is obvious and it is all too easy to give specific names to samples that "merely represent different parts of a normal distribution curve of antigen strength" (Race and Sanger).

Wiener (1953) has even suggested that "A_4" is not a form of A at all but is a group C. The use of such nomenclature which is so distressing to the layman when he first encounters it will be discussed later, but just to complete the confusion it may be added that an alternative explanation of some of these weaker form within the ABO system is that "modifying genes" are operating; these will also be discussed later.

Two other antigens within the ABO system which have also been claimed are referred to as A_m and A_g. The first of these was announced by Wiener and Gordon (1956) in a paper entitled "A hitherto undescribed human blood group" but Race and Sanger suggest that the case described may be explained on the basis of the operation of "modifying genes".

The antigen A_g was described by van Loghem et al., (1957) but again it is doubtful whether a distinct antigen is really involved. The patient had originally been grouped as A without apparent difficulty, but within a year his cells reacted so weakly that they were at first believed to be O. The patient was in fact suffering from myeloblastic leukaemia from which he subsequently died, and it is possible that the reaction of his red cells was being affected by his disease, an explanation which is strengthened by the more recent report by Stratton et al, (1958) of a somewhat similar change occurring in a patient suffering from hypoplastic anaemia.

Whilst it is possible therefore that there are several sub-groups caused by allelic forms of the A gene, attempts to demonstrate additional sub-groups caused by allelic forms of the B gene have not been so successful. Moullec et al., (1955) have however reported the existence of a weak variant B which they call B_3 since its agglutination reactions resemble those of A_3. It is inherited as a single dominant gene, but there appear to be no figures available relating to its frequency; it may be presumed to be very rare.

Levine et al., (1958) describe another phenotype B_w which reacts very weakly and which, on other grounds, seems to be analogous to A_3. It is also inherited as a single dominant gene, whilst Dunsford et al., (1957) have described an even weaker variety known as B_x which appears to be inherited in the same way. Finally mention should be made of an anomalous variety of B reported by Armstrong et al., (1957). This was discovered in an hermaphrodite whose cells reacted as group O but whose serum lacked anti-B and whose saliva contained the B substance. Whether this is an abnormality associated with hermaphroditism does not appear.

The above mentioned ABO variants appears to cover all those described at the date of writing. It must be admitted that few, if any of them have much medico-legal significance at the moment. Most of them are too insecurely based to be of much value for this purpose and in any case few laboratories would be capable of testing for such variants. It is however worthwhile mentioning them for two main reasons. First, they provide a striking illustration of the complexity which blood group systems are rapidly attaining. Second, bare mention of them at least introduces the nomenclature employed which is some guide to those who attempt to read the literature

without any extensive acquaintanceship with the subject.

An attempt has been made to explain the existence of sub-groups within the ABO system on a single comprehensive theory by Hirszfeld. Consideration of this theory involves discussion of the more recent work on the nature of group O and it will therefore provide a useful bridge between our discussion of the two main lines of development within the ABO system.

In formulating this theory Hirszfeld takes as a starting point Bernstein's suggestion that O,A and B are expressions of mutations of a single gene and states:

> "It seems reasonable to assume that the mutations which led to the appearance of different blood groups had not been complete, but that they have produced many transition forms. Accepting the hypothesis of the O group as the point of departure, it is safe to suppose there is a variable residuum of O-antigen in the mutants which express correspondingly incomplete mutation."

On the basis of experimental work by himself and his collaborator he claimed to be able to distinguish not only a series of mutations, which he called "pleiades" from A_1 to A_5 but also to distinguish between three pleiades within the A_1 group. He also claimed to have demonstrated that the same principles applied to B as to A. He thus constructed a theory of transitional blood groups arising by way of incomplete mutations from O in the direction of A and B, a theory which is well illustrated by the diagram reproduced in Fig.9.

It is now clear, however, that whatever else may be said about the theory it needs modification in so far as it regards O as the starting point for the various mutations. Apart from this, however, at least one person has found it a very stimulating idea although it does not appear to figure very prominently in recent textbooks on the subject. It is obvious, of course, that it cannot be regarded as a complete explanation of all ABO

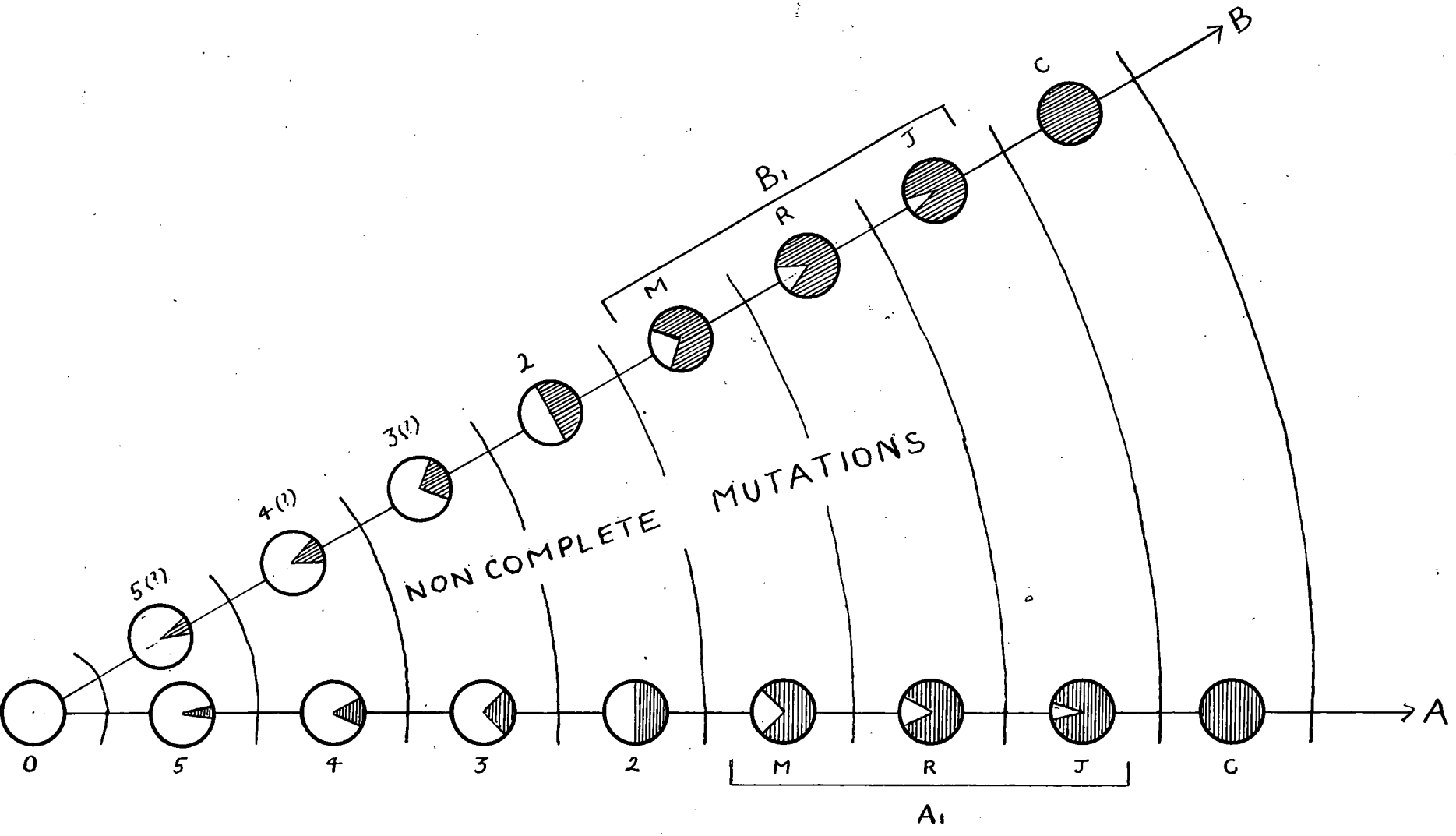


Fig. 9

variants since other factors are manifestly at work, but equally well it may be an explanation of some of the variants.

We turn now to consider the more recent developments in the concept of group O. The classical theory regarded group O as being characterised merely by the absence of A and B antigens and further assumed the complete dominance of A and B over O with the consequence that the homozygote would be indistinguishable from the heterozygote. Bernstein's theory of three allelomorphic genes, however, always carried the possibility that group O was capable of more positive definition than mere absence of A and B. Indeed the first suggestion that group O could be so defined actually preceded the announcement of Bernstein's theory (1924) for in 1921 Hocker and Anderson produced a so-called "anti-O" serum from a rabbit by immunisation with human O cells, and in 1926 Lendsteiner and Witt and Landsteiner and Levine demonstrated an "irregular" isoagglutinin in the serum of A_1 and A_1B individuals which reacted weakly with O cells.

Most development in this field took the form of a search for animal sera with anti-O properties. Schiff (1927) and Greenfield (1928) found that normal cattle sera, after absorption with A and B strongly agglutinated O cells and in 1930-31 Eisler reported the formation of a powerful anti-O agglutinin in goats after immunisation with Shigella dysenteriae, whilst in 1945 Morgan and Waddell produced an anti-O serum by immunisation of rabbits with a preparation of O-substance obtained from pseudomucinous ovarian cyst fluid of group O persons. Meanwhile reports of isoagglutination of O cells

had been increasing (Weiner et al,(1941); Dockeray and Sachs (1941) and Henry (1946)).

Attempts were made to explain these reactions on the basis of heterozygosity on the assumption that the so-called anti-O sera were genuinely anti-O and that the A and B cells which were agglutinated by them were heterozygous AO and BO. (The same explanation was also advanced in respect of the ability of the anti-O sera to agglutinate A_2 cells on the basis that A_2 was a weaker gene than A_1 and was therefore less able to suppress the properties of the O-group in the heterozygous form than A_1 - it was actually this problem which led Hirszfeld to his theory of transitional forms within the ABO system).

The explanation based on heterozygosity of the reactions of the anti-O sera was exploded by Moureau (1937). Later work by Moureau (1946) indicated that the antigen recognised by the goat or ox anti-O was not controlled by Bernstein's third gene.

A major advance was made in 1948 when Morgan and Watkins demonstrated that the so-called anti-O sera could be divided into two groups known as anti-H and anti-O; the factor which was being recognised by the goat and ox antisera was in fact H and not O. The anti-O sera are those which specifically recognise the product of Bernstein's third gene a few of which have been described in the literature. One such was that reported by Boorman, Gilby and Dodd, a powerful human anti-O serum (Mrs. G.) which was found to be specific for both O and A_2.

The proof that the serum "Mrs G." was specific for O as well as A_2 depends upon calculations of theoretical gene frequencies, comparing the observed results with those calculated and assessing the statistical significance of the discrepancies. Methods used for the calculation of gene frequencies will be discussed later; for the present we merely append a simplified form of the findings of Boorman et al., so that the nature of their results may be seen.

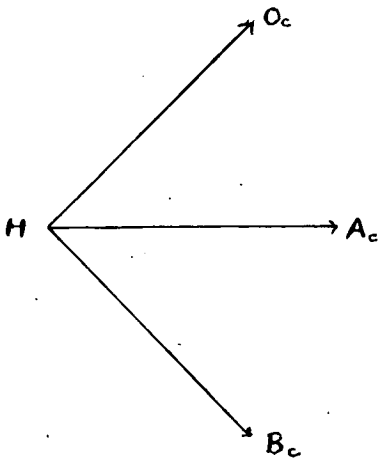
Phenotype	Genotype	Reaction	Observed	Expected
O	OO	-	214	214.00
A_1	A_1O A_1A_2	-	151	155.89
A_1	A_1A_1 A_2O	-	21	22.012
A_2	A_2A_2	-	62	62.00
B	BO	-	32	30.886
B	BB	-	0	1.114
A_1B	A_1B	-	12	9.906
A_2B	A_2B	-	8	4.19
Total			500	499.998

Source: Boorman, Gilby and Dodd (1948)

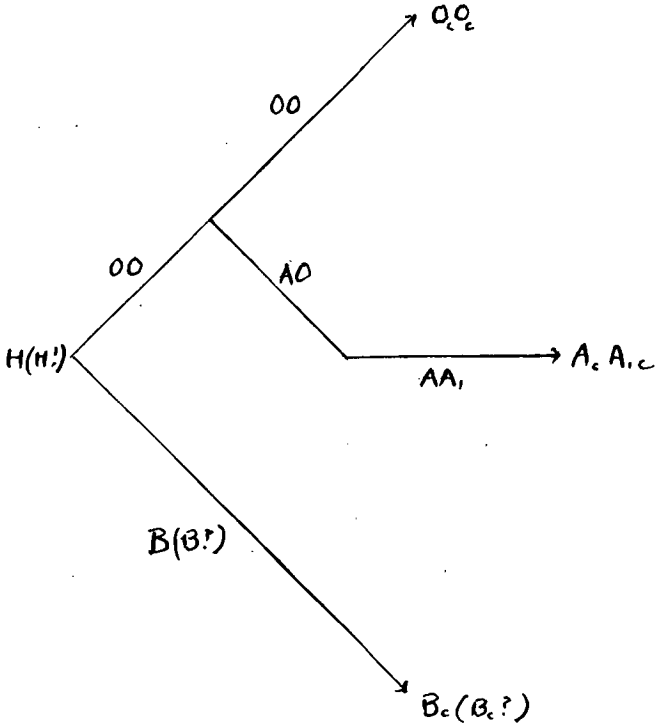
It will be noted that the use of this serum increases the number of groups within the ABO system to eight, it being possible to distinguish between the heterozygous and homozygous B and A_1 groups. Despite the convincing character of their results, and although in their first edition Race and Sanger wrote that the results/"appeared to establish beyond doubt that the

antiserum would agglutinate cells homozygous or heterozygous for the gene O and the gene A_2" the same authors, in their third edition appear sceptical and "do not feel confident of the existence of any serum capable of making this distinction." It must, it seems, remain an open question whether any genuine anti-O serum has been reported, and we are therefore left with the anti-H sera which requires a few brief comments.

The first point which may be made is that it is the discovery of the H-substance that has required some modification of Hirszfeld's transitional forms theory for it now seems clear that if the A and B antigens have arisen by way of mutation it is from H rather that from O that they have arisen. Two such modifications have been proposed; one by Morgan and Watkins (1948), the other by Boorman, Dodd and Gilby (1948). They are sufficiently illustrated by the following diagrams:



Morgan & Watkins



Boorman, Dodd & Gilby

It is quite clear, however, that these modifications do not represent anything like a final solution of the many problems involved. There remains, for example, the puzzling fact that there are now known to be three "substances namely, A, B and H and three genes controlling the basic ABO system. Nevertheless there is no symmetry between the two, for there is no known O-substance corresponding with the A and B substances. This is a problem which is best discussed in connection with the "secretor system" which will be dealt with later.

The conclusion which emerges from the above discussion is that the status of the O-group is still very undetermined. Whether it can yet be defined otherwise than negatively, as absence of the antigenic properties of A and B depends upon whether any genuine human anti-O serum is discovered. Race and Sanger are pessimistic: "We do not expect such a serum to be found".

We turn now to consider a few factors which still further complicate the ABO system. The first of these concerns the so-called "cross-reaction" of anti-A and anti-B. The problem here is to ~~explicit~~ explain the curious phenomenon (first described by Hektoen in 1907) that A cells can combine with β and B cells with α when mixed with O serum although no such phenomenon is encountered if an artificial mixture of A and B sera is used.

Race and Sanger list two alternative explanations of this phenomenon. The first is that the antibody molecules in the serum of group O individuals, although for the most part α or β can occur in a combined $\alpha\beta$ form, and it is these combined molecules which are responsible for the fact that group A cells after being mixed with group O serum give up, on elution, some α as well as β. This would account for the fact that "cross-reaction"

does not occur if an artificial mixture of A and B sera is used, for in this case the antibody molecules would only occur in the uncombined state.

The second explanation is that group O persons possess a third antibody in their serum, anti-C, for which A, B and AB individuals have the corresponding antigen (C) on their red cells. The work of Dodd (1952) and Milgrom (1952) seem to tell against the C: anti-C interpretation of the phenomenon. Milgrom has suggested that it is possible that antibodies may be trivalent, so that in the serum of a group O person the following antibodies would be present.

$\alpha\alpha\alpha$ $\alpha\alpha o$ $\alpha\alpha\beta$ αoo $\alpha o\beta$ $\alpha\beta\beta$ βoo $\beta\beta o$ $\beta\beta\beta$

There is, clearly, no immediate medico-legal significance in these researches at the moment. They are mentioned here primarily as a means of explaining the concept of "group C" to which references are often found in the American literature but which, without explanation, are very confusing to the neophyte.

We now turn to consider the remaining complication of the ABO system, that resulting from the operation of "modifying genes". In 1951 Bhende et al., described a "new" blood group characteristic related to the ABO system. The propositus was remarkable in that his serum contained anti-A, anti-B and anti-H, whilst the red cells were agglutinated by neither anti-A, anti-B, anti-O nor anti-H. The phenomenon was originally explained as being due to an additional allelomorph at the ABO locus, but in 1952 Ceppelini suggested that an inhibitory mechanism was at work, a suggestion which was proved correct by Levine et al., (1956).

The current interpretation of these cases is that there is a rare gene (x) which is independent of the ABO locus and which in the homozygous state prevents the B and O genes from operating i.e. from causing the corresponding antigen to appear on the red cells. There is no information available as yet on the effect of (xx) on the production of the A antigen. The rarity of this type of blood is shown by the fact that Bhatia et al., (1955) failed to find a single example in tests on over five thousand unselected group O individuals. It should be noted in conclusion that the inhibitory mechanism is related in some way to the secretor system, a matter which will be discussed when the secretor system itself is considered.

In 1957 Weiner et al., reported the existence of a very rare gene (y) which in the homozygous state inhibits the development of A antigen in the red cells. It is to this phenotype that Race and Sanger have given the name A_m on the assumption that it is the same as that reported by Weiner and Gordon (1956). They also suggest that Gammelgaard's A_x is probably of the same type. The Yy genes are independent of the ABO locus. As yet, however, there is little information as to the operation of these genes.

The ABO blood group system has clearly developed very considerably in the last few years. From the classical four groups there has been a gradual proliferation of sub-groups with a fog of increasing density settling over the nature of group O. Despite all the uncertainties, however, the four classical sub-groups and the two main sub-groups remain firmly established and available for medico-legal work.

One final matter to which reference should be made, namely the possibility of still further sub-divisions of the ABO system based on the work of Friedenreich and Witt (1933) among others, as mentioned by Kabat, Blood Group Substances, (1956) but not by most other recent writers.

These workers found that whilst anti-B in human serum could be completely absorbed by some animal red cells, it was only partially absorbed by other red cells. Thus whilst rabbit red cells would completely absorb human anti-B, guinea-pig red cells would only absorb a fraction of the anti-B leaving part which could then be absorbed by rabbit red cells. To account for this phenomenon Friedenreich and Witt postulated three factors, all of which were present in normal humans, B_i, B_{ii} and B_{iii}. Similar results have also been obtained in respect of the other antigens of the ABO system. Thus Furuhata (1949, 1954) has suggested the existence of O_i, O_{ii} and O_{iii}, whilst Terajima (cited by Furuhata) indicates the possibility of the existence of an A_i, A_{ii} and A_{iii}. He also suggests that that aspect of the A antigen which acts in a manner similar to the Forssman antigen is really an A_{iv}.

Here we see yet further possibilities for major advances in the ABO system, and only time will show what the true potentialities of this work really are.

There is, however, one final problem which must be discussed in connection with the ABO system before we can move on to discuss the other blood group systems, namely, the problem of the inheritance of the ABO blood groups.

THE INHERITANCE OF THE ABO SYSTEM

The first suggestion that blood groups were inherited characteristics was made by Epstein and Ottenberg (1903). In 1910 von Dungern and Hirszfeld proposed a genetic mechanism for this inheritance, and although the details were subsequently shown to be incorrect by Bernstein (1924) it will be useful to discuss first von Dungern and Hirszfeld's theory as a comparison between it and Bernstein's theory will indicate the methods by which inheritance mechanisms are established.

von Dungern and Hirszfeld's theory proposed two independent pairs of allelomorphic genes:

A ..... for antigen A
a ..... for antibody α
B ..... for antigen B
b ..... for antibody β

The theory was thus endeavouring to account for the inheritance of both antigens and antibodies. On this scheme the four phenotypes would be related to nine possible genotypes as follows:

Phenotypes	Genotypes
AB	AABB, AABb, AaBB, AaBb
A	AAbb, Aabb
B	aaBB, aaBb
O	aabb

Bernstein pointed out that on statistical analysis the theory of von Dungern and Hirszfeld did not come up to expectancy since the actual frequency of distribution of the blood-groups did not conform to that which would be expected if the inheritance really depended upon two pairs of allelomorphs. First it is necessary to set out the method by which the expected frequency of distribution can be calculated.

Let p = frequency of A
q = frequency of a

Let r = frequency of B
s = frequency of b

Now by definition $p+q = 1$ and
$r+s = 1$

and the possible combination of these factors is given by the equation

$$(p + q)^2 (r + s)^2 = 1$$

Bearing the above equations in mind let us now consider the blood group O. As was shown above this phenotype comprises but one genotype (aabb). Now the frequency of (aa) and will q^2 for the frequency of (a) is given by q and qq results from the union of two germ cells each bearing the gene q. In the same way the frequency of (bb) will be s^2 and consequently the frequency of the genotype (aabb) and therefore of the phenotype O will be q^2s^2.

Turning now to consider the phenotype AB it can be seen, by the same reasoning, that the frequency of the genotype (AABB) will be p^2r^2. The frequency of the other genotypes within this phenotype must, however, be calculated slightly differently. Consider the genotype (AaBb). Aa may result in one of two ways: either by the union of a sperm carrying A and an ovum carrying a, or of a sperm carrying a and an ovum carrying A. The frequency of the first event is given by pq. Equally, however, the frequency of the second event is also given by pq, so that the frequency of (Aa) will be given by 2pq. By parity of reasoning it can be seen that the frequency of Bb will be 2rs. As a consequence the frequency of the genotype (AaBb) will be 2pq.2rs. By similar reasoning the frequency of all the other genotypes can be established, and the results may be summarised as follows:

	AA p^2	2Aa 2pq	aa q^2
BB r^2	AABB p^2r^2	2AaBB $2pqr^2$	aaBB q^2r^2
2Bb 2rs	2AABb $2p^2rs$	4AaBb 4pqrs	2aaBb $2q^2rs$
bb s^2	AAbb p^2r^2	2Aabb $2pqs^2$	aabb q^2s^2

Source: Snyder.

On the basis of these genotype frequencies the phenotype frequencies can be computed arithmetically as follows:

$$AB = AABB + AABb + AaBB + AaBb$$
$$= p^2q^2 + 2p^2rs + 2pqr^2 + 4pqrs$$
$$= pr\,(pr+2ps + 2qr + 4qs)$$
$$= pr\,(p + 2q)\,(r + 2s)$$

But $p + q = 1$ and $r + s = 1$

Therefore

$$AB = pr\,)1 + q)\,(1 + s)$$
$$= (1 - q)\,(1 - s)\,(1 + q)\,(1 + s)$$
$$= (1 - q^2)\,(1 - s^2) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Considering the phenotype A we can see that

$$A = AAbb + Aabb$$
$$= p^2s^2 + 2pqs^2$$
$$= s^2 (p^2 + 2pq)$$
$$= s^2 (1 - q^2) \quad \ldots\ldots(2)$$

By parity of reasoning it can be shown that the frequency of the phenotype B is $q^2 (1 - s^2)$ $\ldots\ldots(3)$

whilst the frequency of the phenotype O is the same as that of its sole genotype, namely, $O = q^2s^2$ $\ldots\ldots(4)$

From equations (2), (3) and (4) the gene frequencies q^2 and s^2 can be calculated. Thus substituting (4) in (2):

$$A = \frac{O}{q^2}(1 - q^2)$$
$$= \frac{O - Oq^2}{q^2}$$
$$O - Oq^2 = Aq^2$$
$$O = Aq^2 + Oq^2$$
$$= q^2(A + O)$$
$$q^2 = \frac{O}{O + A} \quad \ldots\ldots(5)$$

By substituting (4) in (3) and by similar reasoning it can be shown that

$$s^2 = \frac{O}{O - B} \quad \ldots\ldots(6)$$

Finally by substituting (5) and (6) in (1) we obtain the equation

$$AB = \left\{1 - \frac{O}{O - A}\right\} \times \left\{1 - \frac{O}{O - B}\right\} \quad \ldots\ldots(7)$$

Equation (7) gives a figure for the frequency of group AB which can be compared with the actual frequency observed and thus provide a check upon the accuracy of the theory. An alternative method of proceeding is to

note that $O + AB = q^2s^2(1 - q^2)(1 - s^2)$ .....Equations (1) & (4)
and also that $A + B = q^2s^2(1 - q^2)(1 - s^2)$.....Equations (2) & (3)
so that $O + AB = A + B$ or rather it should hold true if the theory from which it is derived is correct.

In 1924 Bernstein came to the conclusion that the observed distribution frequencies were not in accord with von Dungern and Hirszfeld's theory and he proposed the now familiar triple allelomorph theory. A notable feature of this theory, as compared with that of von Dungern and Hirszfeld, is that it takes account only of the antigens and makes no attempt to include the antibodies. Since, with the exception of the natural antibodies with no known antigenic stimulus, antibodies are produced only in response to immunisation, this was not an unreasonable supposition, as events have proved.

Bernstein's theory can be subjected to the same statistical treatment as von Dungern and Hirszfeld's with the following results: As we have already noted on Bernstein's theory the four basic ABO phenotypes are related to six possible genotypes

Phenotypes	Genotypes
AB	AB
A	AA, AR
B	BB, BR
O	RR

On the basis of this theory the expected frequency distribution can be calculated as follows:

Let p = frequency of A

q = frequency of B

r = frequency of R

Now by definition $p + q + r = 1$

and the possible combination of these factors is given by the equation

$(p + q + r)^2 = 1$

The genotype frequencies can be calculated on the same principles as those used above in discussing Hirszfeld's theory, and the results may be summarised in much the same way:

	A p	B q	O r
A p	p^2	$2pq$	$2pr$
B q	$2pq$	q^2	$2qr$
O r	$2pr$	$2qr$	r^2

On the basis of these genotype frequencies the phenotype frequencies can be calculated arithmetically as follows:

$$AB = 2pq \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$A = p^2 + 2pr \quad \ldots\ldots\ldots\ldots\ldots (2)$$

$$B = q^2 + 2qr \quad \ldots\ldots\ldots\ldots\ldots (3)$$

$$O = r^2 \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

From these p,q and r can be calculated very simply:

$$O + B = r^2 + 2pq + q^2$$
$$= (r + q)^2$$

Therefore $r + q = \sqrt{O + B}$

$$1 - p = \sqrt{O + B}$$

Therefore $$p = 1 - \sqrt{O + B} \quad \ldots\ldots\ldots (5)$$

By parity of reasoning it can be shown that

$$q = 1 - \sqrt{O + A} \quad \ldots\ldots\ldots\ldots (6)$$

whilst, of course,

$$r = \sqrt{O} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

By substituting equations (5) and (6) in (1) we obtain the relationship:

$$AB = 2\left(1 - \sqrt{O + B}\right)\left(1 - \sqrt{O + A}\right)$$

By comparing the actually observed frequency distribution of AB with the value calculated from the above equation a measure of the accuracy of the theory can be obtained. An alternative method is to proceed from the relationship $p + q + r = 1$ and substitute therein the results from equations (5), (6) and (7) so that a further measure of the accuracy of the theory is provided by the relationship

$$\left(1 - \sqrt{O + B}\right) + \left(1 - \sqrt{O + A}\right) + \sqrt{C} = 1$$

Using the figures quoted earlier for the observed frequency distribution of the four blood groups we can now proceed to a statistical comparison of the two theories.

Observed AB	Calculated	
	$AB = \left(1 - \frac{O}{O + B}\right)\left(1 - \frac{O}{O + A}\right)$	$AB = 2\left(1 - \sqrt{O+A}\right)\left(1 - \sqrt{O+B}\right)$
0.0297	0.07725	0.03193

Source: Hanley (1944) adapted

The accuracy of Bernstein's theory is therefore strongly supported by the observed frequency distribution of the four groups.

In practice, of course, the observed frequencies never correspond exactly to that calculated for no test sample is ever absolutely representative of the population from which it is drawn, i.e., in practice $p + q + r$ will never exactly equal 1. Various methods have therefore been developed for

obtaining improved estimates of gene frequencies. One method, also developed by Bernstein results in the following formulae:

$$h = (1 + \tfrac{D}{2})(1 - \sqrt{O+B})$$

$$q = (1 + \tfrac{D}{2})(1 - \sqrt{O+A})$$

$$r = (1 + \tfrac{D}{2})(\sqrt{O} + \tfrac{D}{2})$$

where $D = \sqrt{O+A} + \sqrt{O+B} + \sqrt{O} - 1$

Professor Sir Ronald Fisher has developed yet another set of formulae, being those we used to calculate the gene frequencies within Australia, and which are as follows:

$$p = \frac{t - s}{v} \qquad q = \frac{u - s}{v} \qquad r = \frac{s}{v}$$

where $s = \sqrt{O}$

$t = \sqrt{O + A}$

$u = \sqrt{O + B}$

$v = t + u - s$

There is a further test which can be applied to the two theories, a test which brings us to one of the fundamental aspects of the medico-legal significance of blood-group testing. This is the test of family data. We have already emphasised that no child can possess any gene (other than one arising by way of mutation) that is not possessed by either of its parents. On the basis of the ABO blood-group system, therefore, all possible marriages can be classified according to the blood groups of the two parties, and in the case of each type of marriage the blood groups that the offspring thereof can have can be ascertained. Now with regard to the possible blood-groups of offspring the theories of von Dungern and Hirszfeld and that of Bernstein

lead to different results, so that once again the expected results can be compared with the observed results as a check on the accuracy of the two theories.

On the von Dungern and Hirszfeld theory the four phenotypes are related to nine possible genotypes so that the various ABO matings with their possible offspring appear as follows:

Matings		Children	
Phenotype	Genotype	Possible	Impossible
AB x AB	AABB x AABB AABB x AABb AABB x AaBB AABB x AaBb AABb x AaBb AABb x AaBB A^{A}Bb x AaBb AaBB x AaBB AaBB x AaBb AaBb x AaBb	AB,A,B,O	NONE
A x AB	AAbb x AABB AAbb x AABb AAbb x AaBB AAbb x AaBb Aabb x AABB Aabb x AABb Aabb x AaBB Aabb x AaBb	AB,A,B,O	NONE
B x AB	aaBB x AABB aaBB x AABb aaBB x AaBB aaBB x AaBb aaBb x AABB aaBb x AABb aaBb x AaBB aaBb x AaBb	AB,A,B,O	NONE

Matings		Children	
Phenotype	Genotype	Possible	Impossible
O x AB	AABB x aabb AABb x aabb AaBB x aabb AabB x aabb	AB,A,B,O	NONE
A x B	AAbb x aaBB AAbb x aaBb Aabb x aaBB Aabb x aaBb	AB,A,B,O	NONE
A x A	AAbb x AAbb AAbb x Aabb Aabb x Aabb	A,O	AB, B
B x B	aaBB x aaBB aaBB x aaBb aaBb x aaBb	B,O	AB, A
A x O	AAbb x aabb Aabb x aabb	A,O	AB, B
B x O	aaBB x aabb aaBb x aabb	B,O	AB, A
O x O	aabb x aabb	O	AB, A, B

On Bernstein's theory the four phenotypes are related to the six genotypes giving rise to twenty-one genotypically distinct matings, from which, by the application of the principle that no child can possess a gene not carried by either of its parents, the blood groups of the offspring of the various types of mating can be determined. The results

may be summarised as follows:

Matings		Children	
Phenotype	Genotype	Possible	Impossible
A x A	AA x AA AA x AO AO x AO	A, O	B, AB
A x B	AA x BB AA x BO AO x BB AO x BO	A,B,O,AB	NONE
A x AB	AA x AB AO x AB	A,B,AB	O
A x O	AA x OO AO x OO	A, O	B,AB
B x B	BB x BB BB x BO BO x BO	B, O	A, AB
B x AB	BB x AB BO x AB	A,B,AB	O
B x O	BB x OO BO X OO	B,O	A, AB
AB x AB	AB x AB	A,B, AB	O
AB x O	AB x OO	A,B	AB, O
O x O	OO x OO	O	A,B, AB

Comparison between these two tables reveals that there are two main differences:

1) according to Bernstein's theory a group O parent cannot have a group AB child, whilst he or she can on von Dungern and Hirszfeld's theory;
2) according to Bernstein's theory a group AB parent cannot have a group O child, whilst, again, he or she can on von Dungern and Hirszfeld's theory.

This is a matter which can be checked against empirical data, and the results of so doing favour Bernstein's theory.

We must note here, however, a point which will assume some significance later. In explaining anomalous findings in family data it is no uncommon for haematologists to suggest that the child in question is extra-marital. One of the most important medico-legal applications of blood groups is in disputed paternity proceedings. Care must therefore be taken in resorting to the easy explanation of illegitimacy in dealing with anomalous results for otherwise there is a danger that a child might be held illegitimate by the application of a theory which had become established by the simple expedient of dismissing exceptions as due to illegitimacy.

In point of fact the empirical data was inconclusive for many years, for from the literature published prior to 1925 a substantial number of "exceptions" to Bernstein's theory appeared. Subsequently, however, the number of "exceptions" has declined, a phenomenon which Wiener attributes

to the fact that before 1924 when Bernstein's theory was published, the cases did not attract attention and were not therefore retested. The published family data relating to the problem of the validity of Bernstein's theory has been collected by Wiener and Snyder. To collate all the published sources would require more time, more linguistic ability and greater library facilities than we possess. We will therefore content ourselves with reproducing those collations which have already been made.

Wiener (1946) has collated all the published results down to 1941, but only including those studies undertaken between 1924 and 1932 if they included a total of 250 or more children examined. The results are as follows:

Matings	No. of Families	No. of children in each group				
		O	A	B	AB	Totals
O x O	1563	3772	(14)	(9)	0	3795
O x A	2903	2707	3749	(10)	(1)	6467
A x A	1385	556	2538	0	(2)	3096
O x B	1456	1418	(7)	1831	(1)	3257
B x B	554	203	(1)	1009	0	1213
A x B	1200	605	937	771	848	3181
O x AB	530	(8)	633	646	(3)	1290
A x AB	455	0	533	247	312	1092
B x AB	323	(2)	183	406	232	823
AB x AB	59	0	28	36	65	129
Totals	10,628	9,271	8,643	4,965	1,464	24,343

Snyder, (1929) on the other hand lists those investigations into the offspring of O x AB families made between 1910-1929 including those tests which involved only very few families. Following Harley, (1944) we divide the list into a pre-1926 and a post-1926 part, summing the results for each part separately thus

making clear the decline in the frequency of the exceptions:

Investigator	No. of Families	No. of Children			
		AB	A	B	O
V. Dungern & Hirszfeld (1910)	4	3	2	2	2
Learmonth (1920)	3	12	0	0	0
Avdeieva & Grizevicz (1921)	2	1	0	0	2
Keynes (1922)	1	1	0	2	0
Tebbutt & McConnel (1922)	2	0	7	5	0
Ottenberg (1922)	2	0	5	5	0
Oyanada (1922)	3	0	6	0	0
Buchanan (1923)	4	1	2	2	6
Jervell (1923)	3	0	5	2	0
Dyke & Budge (1923)	1	0	0	1	0
Kirihara (1924)	6	0	9	8	1
Plüss (1924)	7	1	8	8	2
Mino (1924)	4	0	5	4	0
Hirszfeld et al. (1924)	1	0	2	0	0
Dossena (1924)	7	0	2	3	2
Furuichi (1925)	9	2	7	7	2
Kawaishi & Furuhashi (1925)	4	2	11	8	2
Staquet (1925)	2	1	9	2	8
Totals 1910-1925	65	24	80	59	27
Sievers (1927)	14	0	30	29	0
Landsteiner & Levine (1928)	6	0	10	11	2
Thomsen (1928)	43	1	50	60	0
Furuhata (1928)	50	0	61	57	1
Vuori (1929)	21	0	36	42	0
Snyder (1929)	15	0	31	35	1
Totals 1927-1929	149	1	218	234	4

Snyder has also analysed the results of the reported results of investigations into the offspring of O x O matings which were carried out between 1910 and 1929 which also includes results excluded from Wiener's table i.e. those involving less than 250 children. We again divide the table into a pre-1926 and a post-1926 period, summing the results for each period separately:

Investigator	No. of Families	Children in Group O	Children in Other Group
v. Dungern & Hirszfeld(1910)	11	25	0
Learmonth (1920)	9	18	1
Keynes (1922)	2	4	0
Tebbutt & McConnel (1922)	5	17	0
Ottenberg (1922)	12	25	0
Buchanan (1923)	8	17	13
Jervell (1923)	2	5	0
Dyke & Budge (1923)	30	30	0
Kirihara (1924)	6	20	0
Pliss (1924)	12	27	0
Mino (1924)	12	31	5
Hirszfeld et al, (1924)	7	19	0
Dossena (1924)	31	31	0
Avdeieva & Grizevicz ( )	16	33	0
Totals 1910-1929	163	302	19
Staquet (1926)	9	35	1
Thomsen (1927)	41	126	1
Sievers (1927)	30	101	0
Kliewe (1928)	5	10	0
Landsteiner & Levine (1928)	34	140	4
Foruhata (1928)	105	216	0
Vuori (1929)	53	154	1
Snyder (1929)	131	516	1
Totals 1926-1929	408	1198	8

A comparison between the incidence of "exceptions" in O x O and AB x O matings is of some interest, for any exceptions in the latter case would be exceptions to both Bernstein's and von Dungern and Hirszfeld's theory and therefore even before 1925 would have attracted attention and probably undergone re-test. The greatest number of exceptions were probably due to faulty technique, operation of weak antigens, not then known and illegitimacy.

One final piece of information which it is worthwhile recording in relation to Bernstein's theory, namely the tabulation, made by Boyd (1939), as to the total incidence of exceptions to Bernstein's theory, which is as follows:

Period of investigation	No. of families	No. of children	Exceptions per 1000 families	Exceptions per 1000 children
1910-1925	973	2270	19.5	13.2
1926	928	2213	1.1	0.47
1927-1930	5018	11141	4	2
1935-1937	541	1473	3.7	2.0

It may be added that if a similar analysis is applied to the results of Wiener's figures, quoted above, involving 24,343 children, and covering the period 1924-1941, the figures are 2.383 exceptions per thousand children and 5.456 exceptions per thousand families.

The last analysis which is worth quoting in support of the Bernstein theory is that undertaken by Wiener, who has collected the published results, over the period 1925-1935, relating to the offspring of Group AB mothers and Group O mothers which shows that the incidence of exceptions is almost negligible.

Blood Groups of Children with Group AB Mothers

Investigators	No. of Mothers	No. of children				
		O	A	B	AB	Total
Ohnesorge (1925)	9	1	3	1	4	9
Rech & Wöhlisch (1926)	7	0	4	2	1	7
Lattes et al., (1928)	13	0	7	6	0	13
Juhasz-Schäffer (1928)	20	0	11	6	3	20
v.Khrenringer-Guggenberger (1928)	7	2	2	2	1	7
Preger (1927)	16	0	8	8	5	21
Thomsen (1927)	65	0	35	30	13	78
Schiff (1927)	102	0	46	33	23	102
Ichida (1929)	15	0	15	7	5	27
Liedborg (1929)	10	0	3	6	1	10
Wolff (1929)	10	0	5	4	1	10
Wiener (1930)	89	0	51	38	22	111
Haselhorst (1930)	57	0	28	17	12	57
Buining (1932)	227	0	168	208	70	446
Wolff & Jonsson (1935)	28	0	17	7	4	28
Totals	675	3	403	375	165	946
Percentages		0.31	42.60	39.64	17.44	100.00

Blood Groups of Children with Group O Mothers

Investigators	No. of Mothers	No. of Children				
		O	A	B	AB	Total
Ohnesorge (1925)	108	85	18	4	1	108
Rech & Wöhlisch (1926)	70	39	22	7	2	70
Lattes et al., (1928)	195	135	41	19	0	195
Juhasz-Schäffer (1928)	147	116	23	12	0	151
v. Khreninger-Guggenberger (1928)	70	52	14	2	2	70
Preger (1927)	139	108	33	11	0	152
Schiff (1927)	788	462	255	71	0	788
Ichida (1929)	26	22	5	9	0	36
Liedberg (1929)	86	52	30	4	0	86
Wolff (1929)	61	39	16	8	0	63
Wiener et al., (1930)	702	465	188	95	0	748
Haselhorst (1930)	492	314	146	34	0	494
Buining (1932)	1274	1265	370	646	0	2281
Wolff & Jonsson (1935)	212	125	63	24	0	212
Totals	4370	3279	1224	946	5	5454
Percentages		60.12	22.44	17.34	0.09	100.00

It may be thought that the point regarding the evidence for and against Bernstein's theory has been unduly laboured particularly since the theory has been unquestioned for so long now. If the point has been laboured, it has been done so deliberately and for two main reasons. First it provides a convenient means of introducing a number of fundamental concepts, and second, it provides a very good illustration of the type of evidence and reasoning upon which the theories of inheritance rest. The application of blood groups in the field of disputed paternity proceedings rests upon the inheritance of blood groups and it is desirable that those who are concerned with such applications of blood group testing should have some idea of the evidence upon which the theories they are applying rest.

So far as the evidence goes, however, it seems quite clear that Bernstein's theory as to the inheritance of the basic ABO system must be regarded as well established and as sufficiently reliable for use in medico-legal disputed paternity problems. Indeed there appears to be only one well authenticated exception so far as the basic ABO system is concerned. This is the case reported by Haselhorst and Lauer (1930) in which a group AB mother had a group O child who was unfortunately a deaf-mute with major deformities, who was also blind. If, as Wiener suggests, this case was due to a recessive mutation, it is not unreasonable to add that the gross congenital deformities suffered by the child could well have resulted from the same cause.

Bernstein's theory, however, has to be modified slightly to allow for the existence of sub-groups within the ABO system. This modification does not in any way involve any reconsideration of the principles discussed above, it is merely an extension of the same principles to cover the situation created by the operation of four rather than three alleles.

Within the A_1A_2BO system there are six phenotypes related to ten genotypes according to the scheme set out earlier.

If p_1 = frequency of A_1

p_2 = frequency of A_2

q = frequency of B

r = frequency of O

then the formulae for the calculation of gene frequencies become:

$$p_1 = \sqrt{O + A_1 + A_2} - \sqrt{O + A_2}$$

$$p_2 = \sqrt{O + A_2} - \sqrt{O}$$

$$q = \sqrt{O + B} - \sqrt{O}$$

$$r = \sqrt{O}$$

and the calculated distribution frequencies correspond satsifactorily with the observed frequencies. The theory of the existence of a fourth gene allelic at the ABO locus is also borne out by family data studies. Within the A_1A_2BO system there are twenty-one possible mating types, and these with the possible phenotypes of their offspring are set out in the following table:

Mating	Children	
	Possible	Impossible
$A_1 \times A_1$	A_1, A_2, O	B, A_1B, A_2B
$A_1 \times A_2$	A_1, A_2, O	B, A_1B, A_2B
$A_1 \times B$	A_1, A_2, B, O, A_1B, A_2B	None
$A_1 \times O$	A_1, A_2, O	B, A_1B, A_2B
$A_1 \times A_1B$	A_1, B, A_1B, A_2B	A_2, O
$A_1 \times A_2B$	A_1, A_2, B, A_1B, A_2B	O
$A_2 \times A_2$	A_2, O	A_1, B, A_1B, A_2B
$A_2 \times B$	A_2, B, O, A_2B	A_1, A_1B
$A_2 \times O$	A_2, O	A_1, B, A_1B, A_2B
$A_2 \times A_1B$	A_1, B, A_2B	A_2, O, A_1B
$A_2 \times A_2B$	A_2, B, A_2B	A_1, O, A_1B
B x B	B, O	A_1, A_2, A_1B, A_2B
B x O	B, O	A_1, A_2, A_1B, A_2B
B x A_1B	A_1, B, A_1B	A_2, O, A_2B
B x A_2B	A_2, B, A_2B	A_1, O, A_1B
O x O	O	A_1, A_2, B, A_1B, A_2B
O x A_1B	A_1, B	A_2, O, A_1B, A_2B
O x A_2B	A_2, B	A_1, O, A_1B, A_2B
A_1B x A_1B	A_1, B, A_1B	A_2, O, A_2B
A_1B x A_2B	A_1, B, A_1B, A_2B	A_2, O
A_2B x A_2B	A_2, B, A_2B	A_1, O, A_1B

As against the above table may be put the summary, made by Wiener, of the published results of family data relating to the sub-groups of the ABO system, showing only ten exceptions in over three thousand children,

and in none of these exceptions does it appear that illegitimacy was ruled out as a possibility, so that the published results may be taken as a sufficient confirmation of the theory.

Mating	No. of Families	CHILDREN						
		O	A_1	A_2	B	A_1B	A_2B	Total
$A_1 \times A_1$	168	79	394	16	0	0	(1)	490
$A_1 \times A_2$	79	52	127	54	0	0	0	233
$A_1 \times B$	120	57	90	8	54	84	6	299
$A_1 \times O$	387	404	695	69	0	(1)	0	1169
$A_1 \times A_1B$	35	0	65	0	19	40	5	129
$A_1 \times A_2B$	16	0	14	9	10	8	2	43
$A_2 \times A_2$	13	13	(1)	26	0	0	0	40
$A_2 \times B$	43	21	0	34	29	0	32	116
$A_2 \times O$	105	124	(4)	163	0	0	0	291
$A_2 \times A_1B$	8	0	18	0	5	(1)	10	34
$A_2 \times A_2B$	3	0	0	3	3	0	1	7
$B \times A_1B$	25	0	15	0	32	16	0	63
$B \times A_2B$	10	(1)	0	10	15	0	6	32
$O \times A_1B$	38	0	55	0	53	0	0	108
$O \times A_2B$	16	0	0	37	27	0	0	64
$A_1B \times A_1B$	2	0	6	0	2	8	0	16
$A_1B \times A_2B$	0	0	0	0	0	0	0	0
$A_2B \times A_2B$	0	0	0	0	0	0	0	0
Total	1068	751	1484	429	249	158	63	3143

It may perhaps be added that the discovery of further sub-groups within the ABO system will lead to the necessity for further extension of Bernstein's theory, provided, of course, that the additional groups are in fact controlled by additional allelic genes at the same locus. Thus the sub-group A_3 appears to be fairly well established, although very rare. As an indication of the way in which Bernstein's theory may be extended to include a fifth allele we give below the equations for the calculation of gene frequencies in such a case:

If p_1 = frequency of A_1

p_2 = frequency of A_2

p_3 = frequency of A_3

q = frequency of B

r = frequency of O

then

$$p_1 = \sqrt{A_1 + A_2 + A_3 + O} - \sqrt{A_3 + A_2 + O}$$

$$p_2 = \sqrt{A_3 + A_2 + O} - \sqrt{A_3 + O}$$

$$p_3 = \sqrt{A_3 + O} - \sqrt{O}$$

$$q = \sqrt{B + O} - \sqrt{O}$$

$$r = \sqrt{O}$$

Alternatively if the theory is to be modified to include a sub-group based on a distinction between B_1 and B_2, then ignoring the A_3 gene the equations will become as follows:

Let p_1 = frequency of A_1

p_2 = frequency of A_2

q_1 = frequency of B_1

q_2 = frequency of B_2

r = frequency of O

then

$$p_1 = \sqrt{A_1 + A_2 + O} - \sqrt{A_2 + O}$$

$$p_2 = \sqrt{A_2 + O} - \sqrt{O}$$

$$q_1 = \sqrt{B_1 + B_2 + O} - \sqrt{B_2 + O}$$

$$q_2 = \sqrt{B_2 + O} - \sqrt{O}$$

$$r = \sqrt{O}$$

The corresponding equations for any other combinations of alleles can be computed on the same principles.

Despite the universal acceptance of the Bernstein theory, from time to time alternatives are proposed. It is hardly necessary to discuss these here, but the following may be noted.

1. Koltsov (1921) proposed a theory based on three allelomorphs the main objection to which seems to be that it makes group AB recessive.
2. Furuhata (1927) proposed a theory which postulated two pairs of completely linked allelomorphs. This theory leads to exactly the same results as Bernstein's theory but on general genetic grounds is not as acceptable as the latter.
3. Kirihara and Haku (1927) and Bauer (1928) suggested partial linkage of two pairs of allelomorphs. The chief objection to this theory is that in time the situation would develop into that envisaged in von Dungern and Hirszfeld's theory: it would then be open to the same objections as the latter.

4. In 1929 Gini proposed another theory based on polyploidy (a type of chromosome mutation arising from failure during meiotic division to reduce the chromosome complement of the gametes to the haploid number so that on fusion of gametes triploid or even tetraploid zygotes may be formed). No actual details seem to be available as to the operation of this theory.

5. The same is also true of the theory proposed by Durken (1932) which is based on "polymerie."

6. We may finally note the theory proposed in 1937 by Matta which involves the three genes O,A and B but requires that they occur four at a time in each individual. The theory is both unorthodox genetically and unsupported by observation.

It is perhaps not without significance that no alternative theory has been proposed for over twenty years. That fact is, in itself, a testimony to the general acceptance of the Bernstein theory.

There is one final point which requires emphasis before we leave the subject of the inheritance of the ABO system. We have already shown that it is possible to determine, in relation to any given type of mating, the possible blood-groups possessed by any offspring thereof. It is therefore possible to state in any given case whether a child could, biologically, be the offspring of any given parents. This is a matter which will be discussed in greater detail later, but for the present it must be noted that it is possible to state this fact in terms of probability i.e. the probability that the child is not the offspring of

the given parents. Such a probability is simply a measure of the degree of accuracy possessed by the theory of inheritance under which the child is excluded. It is also possible to state the probability, in any given case, that the child of any given parents will possess any particular blood group. This however is a totally different thing from the probability that the child in question is or is not the child of the alleged parents, and is mentioned here only for the purpose of emphasising the distinction between the two things, for the distinction has not always been made clear by non-medical writers in this field.

For the purpose of underlining this distinction we propose to discuss briefly the problem of the probability that the child of any given union will possess any given blood group.

Consider the case of an O x O mating, any child which is the offspring of such a union must (mutation apart) be a group O child: we may therefore say that the probability that any child produced from such a union will be group O is 100%, whilst the probability that the child will possess any other group is nil. To take another case, consider an AO x BO mating. As we have seen the blood group possessed by any child of such a union may be any one of four types: AB,AO,BO,OO. Now there is no reason why the child should possess one group rather than another so we may say that the probability that the child will be of group O is 1 in 4 (25%). Thus the probability of any given blood group resulting from any given union can be calculated. The figures for the basic ABO

system may be tabulated as follows:

Matings	Probability of child possessing blood-group					
	AA	AO	BB	BO	AB	OO
AA x AA	1.00	—	—	—	—	—
AA x AO	0.50	0.50	—	—	—	—
AO x AO	0.25	0.50	—	—	—	0.25
AA x BB	—	—	—	—	1.00	—
AA x BO	—	0.50	—	—	0.50	—
AO x BB	—	—	—	0.50	0.50	—
AO x BO	—	0.25	—	0.25	0.25	0.25
AA x AB	0.50	—	—	—	0.50	—
AO x AB	0.25	0.25	—	0.25	0.25	—
AA x OO	—	1.00	—	—	—	—
AO x OO	—	0.50	—	—	—	0.50
BB x BB	—	—	1.00	—	—	—
BB x BO	—	—	0.50	0.50	—	—
BO x BO	—	—	0.25	0.50	—	0.25
BB x AB	—	—	0.50	—	0.50	—
BO x AB	—	0.25	0.25	0.25	0.25	—
BB x OO	—	—	—	1.00	—	—
BO x OO	—	—	—	0.50	—	0.50
AB x AB	0.25	—	0.25	—	0.50	—
AB x OO	—	0.50	—	0.50	—	—
OO x OO	—	—	—	—	—	1.00

The above calculations relate, of course, to the genotypes: the same type of calculations can be made in respect of the phenotypes, although in this case they are rather more complex since account has to be taken of the probable frequency of occurrences of each of the genotypic matings comprising each phenotypic mating. Thus an A x A mating comprises three genotypic matings; AA x AA, AO x AA and AO x AO. In calculating the probability of any given blood group resulting from an A x A mating the probabilities resulting from each of the genotypic matings must be considered together with the frequency with which each of the genotypic matings is likely to occur.

The calculation of the probable frequency of the different mating types is a simple application of the calculated gene frequencies and this type of analysis can be carried through to the extent of calculating the probable distribution of the various blood groups throughout the entire population. Some examples of this type of analysis will be given in connection with some of the simpler blood groups.

The point to bear in mind, however, is that there is a fundamental distinction between calculating the probability of the blood group of a child given the blood group of its parents, and determining, given the blood group of the child and mother, the possible blood groups that could have been possessed by the father.

DEVELOPMENT OF THE ABO ANTIGENS

The A and B antigens can be detected in foetal blood long before birth. Kemp (1930) has thus detected A in a foetus of but 37 days. Wiener (1946) points out, however, that the subgroups of A are not so well developed and even at birth there may be difficulty in differentiating between A_1 and A_2.

Nothing very reliable, however, can be said about the development of the O or H antigens. Obviously this is a problem whose solution must await a decision as to whether there is a problem, and if so what is its nature. Thus if there is no O antigen it can have no development. The problem has been investigated by Formaggio (1952) and Watkins (1951) but their results seem to show that the state of development varies according to the antiserum used.

THE MN BLOOD GROUP SYSTEM

As already recounted, the MN blood-group system was discovered in 1927 by Landsteiner and Levine when experimenting with rabbit sera into which human red cells had been injected. In this way they discovered two immune antibodies which were capable of recognising two additional antigens in man. The antigens so discovered were christened M and N, the corresponding antibodies being anti-M and anti-N.

As we shall see shortly, the original theory proposed by Landsteiner and Levine, that of two allelic genes, is generally accepted. On the basis of this theory it can be seen that there will be three genotypes related to three phenotypes as follows:

Genotype	Phenotype
MM	M
MN	MN
NN	N

The frequency of distribution of the phenotypes can be obtained in the usual way. There appear to have been no tests taken on the white Australian population (although there are some figures available where anti-S has been used which will be referred to later). We therefore quote the relevant English figures:

Group	No.	%
M	363	28.38
MN	634	49.57
N	282	22.05
Total	1279	100.00

Source: Race and Sanger (1958)

As in the case of the ABO system the frequency distribution of the MN blood groups is very different among the Australian aboriginal from that among the European. The following is a summary of the published results:

Group	No.	%
M	101	6.95
MN	486	33.55
N	862	59.50
Total	1449	100.00

Sources:
Birdsell & Boyd (1940)
Wilson et al. (1944)
Simmons et al. (1944)

The most notable feature of these figures is the very low frequency distribution of M, although it should be emphasised that the frequency figures vary not inconsiderably within Australia itself. Thus whilst tests in New South Wales and Victoria have revealed a total absence of M (admittedly the tests were done on relatively small numbers) whereas in the Northern Territory the frequency distribution rises to as high as 11.0%.

Using the phenotype frequency distribution figures the gene frequencies can be calculated. The calculations in this case are extremely simple:

$$M = \bar{M} + \frac{\overline{MN}}{2}$$

$$N = \bar{N} + \frac{\overline{MN}}{2}$$

where M = gene frequency
$\bar{M}$ = phenotype frequency

Substituting the phenotype figures in the above equations we obtain the following results for the gene distribution figures:

M 0.53165
N 0.46835

Using these figures the expected frequency of the phenotypes can be calculated and comparison between the values thus obtained and the phenotype frequencies observed in practice will provide a test as to the "internal consistency" of the results.

MM	=	0.53165^2			=	0.28265
MN	=	0.53165	x	0.46835×2	=	0.49800
NN	=	0.46835^2			=	0.21935

Applying these calculated frequencies to the sample of 1279 from which the phenotypes distribution figures were obtained we obtain the following results

Group	Expected	Observed
M	361.5	363
MN	636.9	634
N	280.5	282
Total	1278.9	1279

This result, as Race and Sanger from whom the above calculations were taken, point out, was better than could reasonably be hoped for.

SUB-DIVISIONS OF THE MN SYSTEM

Although some weak and rare forms of the M and N antigens had been reported earlier the first major development of the MN system occurred in 1947 when Walsh and Montgomery of the New South Wales Blood Transfusion Service discovered a serum which recognised an antigen which although associated with the MN system was distinct from either M or N. The serum was christened Anti-S; the antigen which it was recognising being called S.

For a time the exact relationship of S to the MN system was in doubt but in 1951 this problem was resolved when Levine et al., discovered a further antiserum known as anti-s a discovery which made it clear that S was a separate gene with an allelomorph (s) which was recognised by the antibody discovered by Levine.

Anti-s is still very rare and most tests are therefore confined to anti-M, anti-N and anti-S. The frequency distribution of the phenotypes and genotypes may be obtained in the usual way, but before setting out the results it may be noted that within the MNSs blood group system there are ten genotypes from which six phenotypes can be distinguished by the use of anti-M, anti-N and anti-s. These are as follows:

Genotypes	Phenotypes
MS/MS, MS/Ms	M.MS
Ms/Ms	MsMs
MS/NS, MS/Ns, Ms/NS	M.NS
Ms/Ns	MsNs
NS/NS, NS/Ns	N.NS
Ns/Ns	NsNs

The Australian figures for the frequency distribution of the six distinguishable phenotypes are as follows:

Group	No.	%
M.MS	78	21.67
MsMs	29	8.056
M.Ns	90	25.00
MsNs	89	24.73
N.Ns	21	4.634
NsNs	53	14.72
Total	360	

Sources: Walsh & Montgomery (1947)
Simmons & Graydon (1950)

Again, of course, we find that the frequency distribution figures for the Australian aborigine differ from those for the white population. Tests made by Sanger (1950) on 176 aborigines showed a total absence of M.MS, M.NS and N.NS showing that associated with low M frequency is an almost total absence of S.

From the phenotype frequency distribution figures the gene frequencies can be calculated. Although Ss are not allelomorphs of M or N at the MN locus they are nevertheless so closely linked that each chromosome can be treated for this purpose as though it were a single gene so that the calculations become as follows:

$$Ms = \sqrt{MsMs} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$M = \sqrt{MM} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

therefore

$$\frac{Ms}{M} = \sqrt{\frac{MsMs}{MM}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

but we have already seen that $M = \overline{M} + \frac{\overline{MN}}{2}$ $\ldots\ldots\ldots\ldots\ldots (4)$

therefore substituting (4) in (3) we obtain

$$\frac{Ms}{\overline{MM} + \frac{MN}{2}} = \sqrt{\frac{MsMs}{MM}}$$

$$Ms = \left(\sqrt{\frac{MsMs}{MM}}\right)\left(\frac{MM + MN}{2}\right)$$

The value of MS is derived by difference

$$MS = M - Ms$$

The values of Ns and NS are similarly obtained

(Calculations from Mourant, 1954)

The values thus obtained may be adjusted to take account of the incidence of S and s within the MN group. This can be done by noting that $s = \sqrt{ss}$ and adjusting the values of Ms and Ns so that their sum is equal to (s). This adjustment may be made by multiplying the value of each by $\frac{s}{Ms + Ns}$. The values of MS and NS are then adjusted so that

MS → Ms and NS → Ns retain the values derived from equation (4) and of the corresponding equation in the case of N.

Since the proportion of the Australian population which has been tested is so small we give the gene frequencies calculated by Professor Sir Ronald Fisher, using his maximum likelihood method, and based on 1,419 samples. The results are as follows:

MS	0.2471722
Ms	0.2331303
NS	0.0802080
Ns	0.3894090

From those figures the frequencies of M,N, S and s can be obtained by simple addition, giving the following results:

M	.0.5303030
N	.0.4696970
S	.0.3273502
s	.0.6726198

FURTHER DEVELOPMENTS OF THE MN SYSTEM

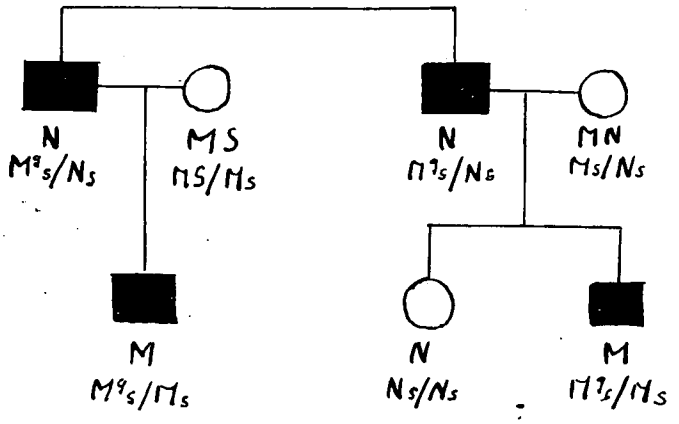
Under this heading we must first refer to a number of rare and weak forms of the M and N antigens. Crono (1935) and Friedenreich (1936) reported the existence of a weak N antigen which is known as N_2. The rarity of the antigen is shown by Andresen (1947) who reported that it had only been found eight times in 20,000 paternity cases. It appears to be controlled by a third allele at the MN locus, in much the same way that A_2 is an additional allele at the ABO locus.

In 1938 Friedenreich and Lauridsen reported the discovery of a weak form of M, known as M_2, whilst in 1949 Jakobowics et al., reported the existence of an additional form of M which was qualitatively distinct from the normal M but no further details are available.

Dunsford et al., (1952) further reported the existence of an antigen known as M^c which is apparently considered to be an antigen intermediate between M and N, but again no further details are available.

Finally note should be taken of the report by Allen et al. (1953) of yet a further allele of M and N known as M^g which is of great rarity having so far been found in only one family, although the anti-body (anti-M^g) appears to be fairly common.

The details of this case are worth considering a little further for it has, as Race and Sanger point out, interesting medico-legal implications. The details of the family are as follows:



As can be seen from the above details on the use of anti-M and anti-N alone both fathers would have been excluded from the paternity of their sons, whereas in point of fact the presence of the extremely rare MS antigen virtually conclusively proves paternity in those cases.

The full significance of a case such as this will be discussed in greater detail later, but it may be emphasised that it provides a very good illustration of the fact that, even from the medico-legal point of view, rare and unusual antigens cannot be left out of account simply on the ground that they are, at the moment, among the curiosities of science.

A further development of the MN system occurred in 1953 with the discovery of a third allele at the S locus, now known as S^u. This was discovered by Wiener et al, who first called it U, and postulated the existence of a pair of allelic genes U and u, but subsequent work by Greenwalt et al, (1954) showed that U was related to the MNS system as an allele at the S locus. An interesting feature of S^u is that negative reactions are only obtained from negroes.

Few figures are available as to the distribution frequency of S^u. The latest figure quoted by Race and Sanger give a gene frequency of 0.0529, and the observed results agree well with those calculated on the basis that a third allele at the S locus is operating.

Finally reference must be made to several antigens which had earlier been described as "private" on the ground of their rarity and lack of indentification with the main blood group systems, but which are now known to be associated with the MNS system. The first of these is the antigen Hu discovered in 1934 by Landsteiner et al, and found to be present in about 7% of American negroes and 22% of West Africans. It occurs but is very rare in Europeans. Although its association with the MNS system clearly follows from the fact that all blood giving positive reactions are found to be either N or MN, the exact nature of the relationship between Hu and the MNS system seems not yet to have been discovered.

In 1951 Klein and Mourant identified another negro antigen, known as He which is found in about 2.7% of West Africans but has not yet been discovered among Europeans. Again the nature of its association with the MNS system, whilst clearly established as a fact, is obscure as to the details.

Three other antigens associated with the MNS system have been reported. The first, known as anti-V^a was discovered in 1951 by Levine et al. The antigen does not occur very frequently, about one in 500 white people giving positive reactions.

The second of these antigens, known as Vw was described in 1954 by van der Hart et al., which appears to be an antigen of rather greater rarity than Mi^a. The discovery that the family in which Vw was first found were also Mi^a positive led to the suggestion that the two were identical. This has been disproved by Wallace et al., (1957) who shows that only about half Mi^a positive people are also Vw positive. The relationship between these two, however, still appears to be an open questions. Mohn et al., (1958) suggests that the phenotype Mi (a+) Vw (+) is due to the presence of a single gene Vw, whilst the phenotype Mi (a+) Vw (-) is due to the presence of the gene Mi^a but that anti-Vw sera contains but one antibody anti-Vw, whilst anti-Mi^a sera contains both anti-Mi^a and anti-Vw. Little more can be added here, for the problem is one which remains to be solved.

Finally reference must be made to the recently described Vr antigen reported by van der Hart et al. (1958) which is apparently associated with the MNS system but regarding which no details are available.

From the simplicity of the MN system with its two antigens M and N much ground has been covered in the last twelve years to reach the present state of complexity in which problems arise more rapidly than their solutions.

INHERITANCE OF THE MN BLOOD GROUP SYSTEM

There has been no dispute regarding the genetic mechanism controlling the inheritance of the MN system comparable with that which arose in connection with the ABO system. The theory originally proposed by Landsteiner and Levine, that of a single pair of allelomorphs, is generally agreed upon and is supported by the available evidence.

A statistical test may be arranged as follows:

Let m = frequency of M

n = frequency of N

so that by definition $m + n = 1$

possible combinations of the factors being given by the equation

$(m + n)^2 = 1$

From the above it follows that

$$MM = m^2$$

$$MN = 2mn$$

$$NN = n^2$$

therefore $m = \sqrt{M}$

$n = \sqrt{N}$

but $m + n = 1$

therefore $\sqrt{M} + \sqrt{N} = 1$

The observed phenotype frequencies can be examined to see whether this relationship holds: if it does the accuracy of the theory is strongly supported. If we apply this test to the English frequency distribution figures we obtain the following results:

Size of sample 1279

MM 0.2838

NN 0.2205

$\sqrt{M}$ 0.5327

$\sqrt{N}$ 0.4696

$\sqrt{M} + \sqrt{N}$ 1.0023

which is a sufficiently good fit under the circumstances.

The family data also supports the theory. With the three phenotypes and genotypes in the system as defined by anti-M and anti-N six matings types are possible, which, with the blood groups which could be possessed by their offspring are set out below:

Matings	Children	
	Possible	Impossible
MM x MM	M	MN, N
MM x MN	M,MN	N
MM x NN	MN	M,N
MN x MN	M,MN,N	None
MN x NN	MN,N	M
NN x NN	N	M,MN

Wiener has collated the published family data, which shows 13 "exceptions" in 6718 children. The results are as follows:

Matings	No. of Families	Children			
		M	N	MN	Total
MM x MM	205	594	0	(3)	597
MM x MN	588	860	(5)	988	1853
MM x NN	226	(1)	(2)	698	701
MN x MN	616	417	361	1094	1872
MN x NN	426	(2)	682	688	1372
NN x NN	104	0	323	0	323
Total	2165	1874	1373	3471	6718

Statistical Test of the Theory of Landsteiner and Levine

Investigation	No. tested	Frequency			$m=\sqrt{M}$	$n=\sqrt{N}$	$m+n$
		MN	M	N			
Landsteiner et al	532	53.6	26.1	20.3	0.5112	0.4502	0.9618
	181	47.5	27.6	24.9	0.5256	0.4990	1.0246
	81	33.33	62.97	3.7	0.7935	0.1924	0.9856
	124	36.29	58.07	5.64	0.7620	0.2376	0.9996
Wiener et al	904	48.23	30.53	21.24	0.5525	0.4609	1.0134
Wiener et al	461	50.32	28.63	21.05	0.5351	0.4588	0.9939
	497	50.71	29.98	19.31	0.5475	0.4394	0.9869
Schiff	1420	49.01	30.14	20.85	0.5489	0.4566	1.0055
	1913	49.77	31.52	18.71	0.5614	0.4326	0.9940
	3333	49.44	30.94	19.62	0.5562	0.4430	0.9992
	180	48.89	23.38	27.78	0.4831	0.5271	1.0102
Shigeno	141	46.81	29.78	23.41	0.5457	0.4837	1.0294
	61	44.26	31.15	24.59	0.5581	0.4958	1.0538
	202	45.80	30.30	23.90	0.5505	0.4889	1.0394
Blaurock	2000	49.1	29.1	21.5	0.5494	0.4637	1.0031
Thomsen et al	442	44.57	29.86	25.57	0.5464	0.5056	1.0520
Lattes et al	430	57.4	27.2	15.3	0.5215	0.3912	0.9127
Kossovitch	400	45.80	33.00	21.20	0.5745	0.4604	1.0349
Crome	1300	49.0	32.5	18.5	0.5701	0.4301	1.0002
Laubenheimer	1000	52.9	27.0	20.1	0.5206	0.4483	0.9682

(adapted from Wiener, 1946)

The family data can be used to give a slightly different check on the Landsteiner and Levine theory, namely that of the distribution of children from the different matings. The theory of this was discussed in connection with the ABO groups. If the six MN mating types are considered then the following distribution of children would be expected:

Mating	Children		
	MM	MN	NN
MM x MM	1.0000	—	—
MM x MN	0.5000	0.5000	—
MM x NN	—	1.0000	—
MN x MN	0.2500	0.5000	0.2500
MN x NN	—	0.5000	0.5000
NN x NN	—	—	1.0000

If this be compared with the results collected by Wiener relating to family data, which were quoted earlier, it will be seen that there is a fairly good fit. There is an apparent excess of MN children, particularly those resulting from MM x MN matings, but Wiener is of the opinion that this may be the result of the use of imperfectly absorbed anti-M and anti-N sera, and he further points out that in the case of MN x MN matings, since all types of children may be expected errors will not be so apparent.

The conclusion is that the single pair of alleles represents the theory that receives overwhelming support from the not inconsiderable body of evidence that has now been collected.

The problem of inheritance of the MNSs system becomes considerably more complex than that of the simple MN system. Following Race and Sanger we will consider the problem from the point of view of S and (s) alone first, before considering the system as a whole.

The gene frequencies of S and (s) have already been given. From these the genotype and phenotype frequencies can easily be calculated:

$$S = 0.5476 \quad \ldots\ldots\ldots \begin{cases} SS = 0.1072 \\ Ss = 0.4404 \end{cases}$$

$$s = 0.4524 \quad \ldots\ldots\ldots \quad ss = 0.4524$$

Since anti-s is a relatively rare serum it is possible, in most cases, only to distinguish between the two phenotypes, and using anti-S alone the family data should conform to the following pattern:

Mating		Children	
Type	Frequency	Proportion of S	Proportion of s
S x S	0.29993	0.03830	0.16170
S x s	0.49546	0.59758	0.40242
s x s	0.20466	—	1.00000

On the assumption that anti-s is available then the situation becomes more complex, but the expected frequency of matings and of the type of issue expected therefrom may be tabulated as follows:

Mating		Children		
Type	Frequency	SS	Ss	ss
SS x SS	0.01149	0.01149	—	—
SS x Ss	0.09444	0.04722	0.04722	—
Ss x Ss	0.19395	0.04849	0.09697	0.04849
SS x ss	0.09699	—	0.09699	—
Ss x ss	0.39047	—	0.19923	0.19923
ss x ss	0.20466	—	—	0.20466

These calculated values may now be compared with those actually observed. Results obtained by testing 1199 children, the offspring of 529 families, with anti-S were as follows:

Mating			Children				
			S		s		
Type	exp.	Obs.	exp.	obs.	exp.	obs.	Total
S x S	158.64	141	265.74	271	51.26	46	317
S x s	262.10	263	354.54	338	238.46	255	593
s x s	108.26	125	0	0	289.00	289	289

Source: Race and Sanger (1958)

The results can be seen to be a good fit. Since very few tests have been done with anti-s the observed results are perhaps not quite so impressive, yet so far as they go they show clear support for the theory. Below are given the results of testing with both anti-S and anti-s 203 children, the offspring of 101 families:

Mating			Children						
Type	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.	Total
SS x SS	1.16	1	3.00	3	—	—	—	—	3
SS x Ss	9.54	17	20.00	18	20.00	22	—	—	40
Ss x Ss	19.59	18	9.75	9	19.50	20	9.75	10	39
SS x ss	9.00	7	—	—	12.00	12	—	—	12
Ss x ss	40.25	39	—	—	41.00	43	41.00	39	82
ss x ss	20.67	19	—	—	—	—	27.00	27	27

Source: Race and Sanger (1958)

Again the results can be seen to be a good fit and sufficient to justify acceptance of the idea that S and s are Mendelian allelic genes.

Having thus considered the inheritance of S and s independently we must turn to consider the inheritance of the whole MNSs system.

The sub-division of the MN system by the use of S and (s) effects a vast increase in the number of mating types that have to be considered. The use of anti-S alone increases the number of phenotypes to six and the number of mating types to twenty-one. With the use of anti-s the number of distinguishable mating types is raised to forty five, out of a total of fifty-five genotypic mating types. In the attached table the various mating types and their offspring, as defined by anti-s, are set out with the addition of a related list of the fifty-five genotypic matings. The distribution frequency of the mating types and their offspring, as thus calculated can be compared with the values obtained from observation. The observed results, as tabulated by Race and Sanger are set out on the second attached table. The results indicate a fairly good fit, bearing in mind that the sample on which the results are based is a relatively small one.

It remains only to consider the simple distribution of phenotypes as a further statistical test of the theory of inheritance (based on a sample of 1419 individuals): (adapted from Race & Sanger, 1958)

Phenotype	Expected	Observed
MN.S.	295.301	295
Ms/Ms	113.751	107
MN.S	393.930	379
Ms/Ns	312.965	322
NN.S	97.788	102
Ns/Ns	215.265	214
Total	1419.000	1419

Once again the results show a good fit.

Matings			Proportion of Children (Phenotypes)					
Phenotype		Genotype	Ms/Ms	MM.S	Ms/Ns	MN.S	Ns/Ns	NN.S
Type	Frequency							
Ms/Ms x Ms/Ms	0.0064	Ms/Ms x Ms/Ms	1.0000	—	—	—	—	—
Ms/Ms x MM.S	0.0032	Ms/Ms x MS/MS Ms/Ms x MS/Ms	0.3481	0.6519	—	—	—	—
MM.S x MM.S	0.0404	MS/MS x MS/MS MS/MS x Ms/Ms MS/Ms x MS/Ms	0.1212	0.8788	—	—	—	—
Ms/Ms/ x Ms/Ns	0.0345	Ms/Ns x Ms/Ns	0.5000	—	0.5000	—	—	—
MM.S x Ms/Ns	0.0887	MS/MS x Ms/Ns MS/Ms x Ms/Ns	0.1740	0.3260	0.1740	0.3260	—	—
Ms/Ms x MN.S	0.0445	Ms/Ms x MS/NS Ms/Ms x MS/Ns) Ms/Ms x Ms/NS)	0.0818	0.4182	0.3468	0.1532	—	—
MM.S x MN.S	0.1116	MS/MS x MS/NS MS/MS x MS/Ns) MS/MS x Ms/NS) MS/Ms x MS/NS MS/Ms x MS/Ns) MS/Ms x Ms/NS)	0.0285	0.4715	0.1207	0.3793	—	—
Ms/Ms x Ns/Ns	0.0243	Ms/Ms x Ns/Ns	—	—	1.0000	—	—	—
MM.S x Ns/Ns	0.0610	MS/MS x Ns/Ns MS/Ms x Ns/Ns	—	—	0.3482	0.6519	—	—
Ms/Ms x NN.S	0.0111	Ms/Ms x NS/NS Ms/Ms x NS/Ns	—	—	0.4533	0.5467	—	—
MM.S x NN.S	0.0277	MS/MS x NS/NS MS/MS x NS/Ns MS/Ms x NS/NS MS/Ms x NS/Ns	—	—	0.1587	0.8422	—	—
Ms/Ns x Ms/Ns	0.0486	Ms/Ns x Ms/Ns	0.2500	—	0.5000	—	0.2500	—
MM.S x Ms/Ns	0.1225	MS/MS x Ms/Ns MS/Ns x Ms/Ns) Ms/NS x Ms/Ns)	0.0409	0.2091	0.2143	0.2857	0.1734	0.0766
MN.S x MN.S	0.0771	MS/NS x MS/NS MS/NS x MS/Ns) MS/NS x Ms/NS) MS/Ns x MS/Ns MS/Ns x Ms/NS) Ms/NS x Ms/NS)	0.0067	0.2433	0.0567	0.4433	0.1203	0.1297
Ms/Ns x Ns/Ns	0.0669	Ms/Ns x Ns/Ns	—	—	0.5000	—	0.5000	—
MN.S x Ns/Ns	0.0842	MS/NS x Ns/Ns MS/Ns x Ns/Ns) Ms/NS x Ns/Ns)	—	—	0.0818	0.4182	0.3468	0.1532
MN.S x NN.S	0.0383	MS/NS x NS/NS MS/NS x NS/Ns MS/Ns x NS/NS) Ms/NS x NS/NS) Ms/Ns x NS/Ns) Ms/NS x NS/Ns)	—	—	0.0371	0.4629	0.1572	0.3428
Ms/Ns x NN.S	0.0304	Ms/Ns x NS/NS Ms/Ns x NS/Ns	—	—	0.2267	0.2733	0.2267	0.2733
Ns/Ns x Ns/Ns	0.0230	Ns/Ns x Ns/Ns	—	—	—	—	1.0000	—
NN.S x NN.S	0.0048	NS/NS x NS/NS NS/NS x NS/Ns NS/Ns x NS/Ns	—	—	—	—	0.2055	0.7945
NN.S x Ns/Ns	0.0209	NS/NS x Ns/Ns NS/Ns x Ns/Ns	—	—	—	—	0.4533	0.5467

Matings			Children											
				Ms/Ms		MM.S		Ms/Ns		MN.S		Ns/Ns		NN.S	
Type	exp.	obs.	Total	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.
Ms/Ms x Ms/Ms	3.39	5	9	9.00	9	—	—	—	—	—	—	—	—	—	—
Ms/Ms x MM.S	17.03	12	32	11.14	7	20.86	24	—	—	—	1	—	—	—	—
MM.S x MM.S	21.37	23	57	6.91	3	50.09	54	—	—	—	—	—	—	—	—
Ms/Ms x Ms/Ms	18.73	30	75	37.50	29	—	—	37.50	46	—	—	—	—	—	—
MM.S x Ms/Ns	46.92	60	137	23.84	25	44.66	53	23.84	19	44.66	40	—	—	—	—
Ms/Ms x MN.S	23.54	15	49	4.01	3	20.49	23	16.99	22	7.51	1	—	—	—	—
MM.S x MN.S	59.04	57	124	3.53	2	58.47	68	14.97	19	47.03	35	—	—	—	—
Ms/Ms x Ns/Ns	12.85	16	39	—	—	—	—	39.00	39	—	—	—	—	—	—
MM.S x Ns/Ns	32.27	24	52	—	—	—	—	18.10	26	33.90	26	—	—	—	—
Ms/Ms x NN.S	5.87	5	7	—	—	—	—	3.17	3	3.83	4	—	—	—	—
MM.S x NN.S	14.65	17	34	—	—	—	—	5.37	4	28.63	30	—	—	—	—
Ms/Ns x Ms/Ns	25.71	28	58	14.50	9	—	—	29.00	34	—	—	14.50	15	—	—
MN.S x Ms/Ns	64.80	67	151	6.13	2	31.57	34	32.36	27	43.14	42	26.18	31	11.57	15
MN.S x MN.S	40.79	29	70	0.47	0	17.03	12	3.97	4	31.03	36	8.42	9	9.08	9
Ms/Ns x Ns/Ns	35.39	28	61	—	—	—	—	30.50	25	—	—	30.50	36	—	—
MN.S x Ns/Ns	44.54	52	112	—	—	—	—	9.16	7	46.84	43	38.84	53	17.16	9
MN.S x NN.S	20.26	14	31	—	—	—	—	1.15	2	14.35	17	4.87	3	10.63	9
Ms/Ns x Ns/Ns	16.08	17	34	—	—	—	—	7.71	11	9.29	11	7.71	6	9.29	6
NN.S x NN.S	2.54	1	1	—	—	—	—	—	—	—	—	0.21	0	0.79	1
Ns/Ns x Ns/Ns	12.17	18	47	—	—	—	—	—	—	—	—	47.00	47	—	—
NN.S x Ns/Ns	11.06	11	19	—	—	—	—	—	—	—	—	8.61	13	10.39	6
Totals	529.00	529	1199		89		268		288		286		213		55

There would be little point in attempting here an equivalent analysis of all fifty-five genotypically distinct MNSs matings. So far as possible offspring are concerned, however, a full analysis, restricted to that point, will be given later when the problems of paternity are discussed.

DEVELOPMENT OF THE MNSs ANTIGENS

The M and N antigens are well developed before birth. Thus Moureau (1935) has grouped foetuses as young as nine weeks. In like manner the S antigen has been detected in a foetus as young as twelve weeks (Race and Sanger 1958).

THE P BLOOD GROUP

The P blood group system was discovered by Landsteiner and Levine (1927) at the same time as they discovered the MN system. Two distinct types of blood were found and were christened P + and P -. As will appear shortly the view taken was that a pair of allelomorphs were responsible and so the two phenotypes are related to three genotypes as follows:

Phenotypes	Genotypes
P +	$\begin{pmatrix} PP \\ Pp \end{pmatrix}$
P -	pp

The only Australian figures for the frequency distribution of phenotypes are those of Simmons and Graydon (1950) who on testing 128 individuals found the following values:

P +	70.31%
P -	29.69%

Since the sample used was very small we give, in addition the figures obtained by Henningsen, regarded by Race and Sanger as the most reliable:

Phenotype	No.	%
P +	1849	78.85
P -	496	21.15
Total	2345	100.00

From these figures the gene frequencies can be calculated very simply for $p = \sqrt{P-}$ and $P = 1 - p$. These equations give the following results:

$$p = 0.4599$$

$$P = 0.5401$$

DEVELOPMENT OF THE P BLOOD GROUP SYSTEM

The first development to be considered involves a point which was noted by Landsteiner and Levine in their original paper, namely that there is a distinction between weakly and strongly reacting P- samples. The real problem is to decide whether these variations in antigen strength follow a normal curve of distribution or whether they represent distinct sub-groups within the P system. The work of Henningsen (1949) suggests that there is no qualitative difference. On the other hand he also suggested that antigen strength appeared to be inherited. Professor Sir Ronald Fisher has established that a partial cause of such variation is heterozygosity, but whether the residual causes are genetic or not appears still to be uncertain.

A further development which took place in 1954 was the recognition that the P system was identical with the Q system which had been reported by Furuhata in 1935; a rare example of a development in blood group serology which engendered a simplification rather than further complication.

Rather surprisingly a similar development took place in 1955 when Sanger showed that the Jay system of blood groups (which had first been described by Levine et al. 1951) was also related to the P system.

The original Jay system was based on a powerful antigen Tj^a which was possessed by the vast majority of people. The antibody, anti Tj^a recognised two phenotypes Tj (a+) and Tj (a-). It was assumed that Tj^a was a Mendelian dominant and that a pair of allelomorphs controlled the system, namely, Tj^a and Tj^b and that therefore there were three genotypes

related to two phenotypes as follows:

Phenotypes	Genotypes
Tj (a+)	Tj^aTj^a, Tj^aTj^b
Tj (a-)	Tj^bTj^b

The gene Tj^b was assumed to be exceedingly rare since no random sample was found in tests of over 10,000 individuals. Once it was discovered that the known Tj(a-) persons were also P- raised the possibility that the two systems were related, for even P- is a relatively rare phenotype. The exact nature of the relationship, however, remains in some doubt. Race and Sanger suggest that in fact the P system is constructed on the same pattern as the A_1A_2O system. Their scheme for the expanded P system is reproduced below:

Antibodies:	Anti-P_1	(previously anti-P)	
	Anti-P - P_1	(previously anti-Tj^a)	
Antigens & Genes:	P_1	(previously P)	previously Tj^a
	P_2	(previously p)	previously Tj^a
	p	(previously Tj^b)	

This scheme gives rise to six possible genotypes related to three possible phenotypes as follows:

Phenotypes	Genotypes
P_1	P_1P_1, P_1P_2, P_1p
P_2	P_2P_2, P_2p
p	pp

It may be added that the resemblance between the P system and the ABO system is still further strengthened by the recent report, Matson et al (1958), of a group which Race and Sanger suggest may be the analogue in the P system of B in the ABO system. The antibody is similar to anti-P - P_1 but the red cells from the paitient react strongly with anti-P_1. It looks as though the P system, for long one of the simplest of human blood groups may soon achieve the complexity of the ABO system.

INHERITANCE OF THE P SYSTEM

No figures are available for inheritance studies to be developed for the expanded P system but those available for the original P system are worth quoting to show that the assumption of a pair of alleles controlling that part of the system seems to be justified.

Taking the P system as defined by anti-P the following distribution of mating types and offspring would be expected:

Matings		Proportion of children	
Type	Frequency	P+	P-
P+ x P+	0.6217	0.9008	0.0992
P+ x P-	0.3336	0.6850	0.3150
P- x P-	0.0447	0.0000	1.0000

Taking the genotypically different matings, then their frequency, with that of their offspring is as follows:

Matings		Children		
Type	Frequency	PP	Pp	pp
PP x PP	0.0851	0.0851	—	—
PP x Pp	0.2898	0.1449	0.1449	—
Pp x Pp	0.2468	0.0617	0.1234	0.0617
PP x pp	0.1234	—	0.1234	—
Pp x pp	0.2102	—	0.1051	0.1051
pp x pp	0.0447	—	—	0.0447

These calculated frequencies may be compared with the observed results, showing a satisfactory fit. The collated results of the published family data studies are tabulated below.

Mating			Children				
			P+		P-		Total
Type	obs.	exp.	obs.	exp.	obs.	exp.	
P+ x P+	933	952.3	2261	2308	301	254.1	2562
P+ x P-	506	511.1	987	1035	523	475.6	1510
P- x P-	96	68.5	5	0	275	280.0	280
Total	1532	1531.9	3253	3343	1099	1010.7	4352

Sources: Henningsen (1950)
Dahr (1942)
Jungmichel (1942)
Moharram (1942)
Sanger et al (1949)
Grosjean (1950) and (1952)
Brendemoen (1952)
Wiener (1953) quoted in Race and Sanger (1958)
Race et al (1953)

DEVELOPMENT OF THE P ANTIGENS

Adopting the nomenclature appropriate to the expanded P system it appears that P_1 is not always fully developed at birth (Henningsen, 1949) although Race and Sanger (1958) apparently had no difficulty in detecting P_1 in a foetus as early as 12 weeks. The same workers also found that P_2 was well developed in the cord blood.

THE RH BLOOD GROUP SYSTEM

The circumstances leading to the discovery of the Rh blood group system have already been recounted. The original antibody (now known as anti-D)divided human blood into two phenotypes known as Rh+ and Rh-. The Australian figures for the frequency distribution of these two phenotypes (Jakobowicz and Bryce 1944) are as follows:

Phenotype	Number	%
Rh+	4582	82.29
Rh-	986	17.71
Total	5568	100.00

On the assumption that the gene responsible for Rh+ is a dominant Mendelian characteristic the gene frequencies can be calculated in the usual way:

$$rh = \sqrt{0.1771} = 0.4208$$

$$Rh = 1 - \sqrt{0.1771} = 0.5792$$

The corresponding genotype frequencies will be:

$$rhrh = (0.4208)^2 = 17.71$$
$$Rhrh = 2 \times 0.4208 \times 0.5792 = 48.74$$
$$RhRh = (0.5792)^2 = 35.56$$
$$100.00$$

a result which indicates reasonably good internal consistency.

The corresponding English figures which may be quoted by way of comparison are set out in the following table.

Investigation	Number tested	Rh+		Rh-	
		No.	%	No.	%
Boorman et al.(1942)	1610	1371	85.16	239	14.84
Race et al. (1943)	4618	3896	84.37	722	15.63
Plaut et al. (1945)	2944	2472	83.97	472	16.03
Discombe (1952)	10000	8278	82.78	1722	17.22
Rice (1952)	5000	4116	83.32	884	17.68
Dunsford (1953)	1206	988	81.92	218	18.08
"	2583	2138	82.77	445	17.23
"	1258	1076	85.33	182	14.47
"	787	655	83.23	132	16.77
"	916	781	85.26	135	14.74
Total	30922	25771	83.33	5151	16.67

Using these figures the gene frequencies may be calculated giving the following results:

$$rh = 0.4083$$
$$Rh = 0.5917$$

and checking the internal consistency of the figures we obtain the following genotype frequencies:

$$rhrh = (0.4083)^2 = 16.67$$
$$Rhrh = 2 \times 0.4082 \times 0.5917 = 48.32$$
$$RhRh = (0.5917)^2 = \underline{35.01}$$
$$100.00$$

The corresponding figures for the aboriginal population (Simmons et al. 1944) based on tests of 281 individuals show 100% Rh+.

The Rh system did not long remain in this state of pristine simplicity. Within a few years further antibodies had been discovered, but until 1944 there was no indication of the nature of their inter-relationship. In 1944, however, Professor Sir Ronald Fisher produced a generalisation of tremendous organising power. He showed that the results then available could be explained on the basis of three pairs of allelic genes closely linked on the chromosome which he named C,c; D,d and E,e. At that date only four of the six genes had been

discovered, namely, C,c, D and E and spectacular confirmation of the theory was provided when the other two predicted antigens were discovered; e by Mourant (1945) who demonstrated the existence of anti-e and d by Diamond (1946). It should perhaps be added that some doubt has recently been thrown on whether d has in fact really been identified. This is a matter which will be discussed when further developments in the Rh system are considered, It may be further added that the acceptance of Fisher's theory is not seriously affected one way or the other by the doubt as to whether the d allele has really been identified.

We may pause here to consider the structure of the Rh system as defined by the three pairs of allelomorphs required by Fisher's theory, but before doing so it should be noted that neither this theory, nor the nomenclature associated with it have commended themselves to Wiener who, with Landsteiner, discovered the Rh system. The substance of Wiener's objection to Fisher's theory appears to be that he prefers to distinguish between antigens and "factors", and instead of referring to three closely linked loci he refers to three factors operating within the boundaries of a single gene or genetic locus. The practical consequencies of this distinction appears to be almost non-existent, save that it complicates the exposition of a subject. Since there appears, at the moment at any rate, to be no particular advantage in using Wiener's theory we shall adhere to Fisher's treatment.

In the matter of nomenclature Fisher and Race use a nomenclature based on that of the genes themselves whereas Wiener uses one based on the symbols R, Rh, Hr, and hr with various complicated sub- and super-scripts. Whilst the latter has a certain advantage in that, on the printed page, it occupies less room, it is much less convenient for typing purposes and positively unwieldly when used orally. Quite apart from practical difficulties the Fisher-Race nomenclature is, to the novice at any rate, much easier to handle and is self-explanatory, whereas that of Wiener is quite arbitrary and very clumsy. For these reasons the Fisher-Race nomenclature will be followed here despite the fact that the American Medical Association have recommended that the Fisher-Race nomenclature be discarded. It is unfortunate that no generally agreed standard nomenclature has been adopted for the Rh system as was done in the case of the ABO system as early as 1921, for although Wiener refers to his nomenclature as the "International Nomenclature" the world wide use of the CDE notation, as Race and Sanger point out, contravenes no international agreement.

We may now turn to describe the structure of the Rh system as defined by the three pairs of alleles required by Fisher's theory. Three pairs of alleles can be combined on a chromosome in eight different ways as follows:

	Alternative short notations	
CDE	R_Z	R^Z
CDe	R_1	R^1
CdE	R_Y	r^Y
Cde	R'	r'
cdE	R''	r''
cde	r	r
cDE	R_2	R^2
cDe	R_o	R^o

These eight chromosomes can be paired in 36 different ways giving rise to 36 different genotypes. The number of phenotypes that can be recognised depends, of course, on the number of antisera used for testing purposes. The Rh system may therefore be considered at various levels of complexity. We have already considered the system at the level attained by testing with anti-D alone, and the next level at which it is convenient to consider the system is attained by testing with three antisera, namely, anti-C, anti-D, and anti-E. At this level eight phenotypes are distinguishable, and these, as related to the genotypes are as shown on the following table.

For the purpose of calculating the chromosome and gene frequencies advantage is taken of the fact that of the eight possible chromosome combinations, two of them CDE and CdE are extremely rare and may be ignored. Of the remaining six chromosomes that have to be considered they may be treated as follows:

$$\begin{aligned} \text{C-ve} &= \text{CDe} + \text{Cde} \\ \text{E-ve} &= \text{cDE} + \text{cdE} \end{aligned}$$

This leaves cDe and cde whose sum is equal to the sum of the C-ve and E-ve types. From these groups the following equations can be derived:

$$\begin{aligned} \text{cDe} + \text{cde} &= \text{ce} = \sqrt{\text{ccee}} \\ \text{CDe} + \text{Cde} &= \text{C} = 1 - \sqrt{\text{cc}} \\ \text{cDE} + \text{cdE} &= \text{E} = 1 - \sqrt{\text{ee}} \end{aligned}$$

Genotype	Reaction with anti-		
	C	D	E
CDe/cDE CDe/cdE cDE/Cde cDE/CDE cDE/CdE cDe/CDE cDe/CdE CDE/cdE CDE/cde CDe/CDE CDe/CdE CDE/CDE CDE/Cde CDE/CdE	+	+	+
CdE/cde CdE/cdE Cde/cdE Cde/CdE CdE/CdE	+	-	+
CDe/cDe CDe/cde cDe/Cde CDe/CDe CDe/Cde	+	+	-
cDE/cDE cDE/cDe cDE/cdE cDE/cde cDe/cdE	-	+	+
cdE/cdE cdE/cde	-	-	+
cDe/cDe cDe/cde	-	+	-
Cde/Cde Cde/cde	+	-	-
cde/cde	-	-	-

These equations are, of course, analagous to the equations

$$r = \sqrt{O}$$
$$p = 1 - \sqrt{B + O}$$
$$q = 1 - \sqrt{A + O}$$

which we obtained in the case of the ABO system. This treatment is only possible, of course, by ignoring the two rare chromosomes CDE and CdE. Since the equations are analagous we may apply Bernstein's correction, and where

$$D = 1 - (cc + C + E)$$

we obtain:

$$cDe + cde = \left(\sqrt{ccee} + \frac{D}{2}\right) \times \left(1 + \frac{D}{2}\right)$$
$$CDe + Cde = \left(1 - \sqrt{cc}\right) \times \left(1 + \frac{D}{2}\right)$$
$$cDE + cdE = \left(1 - \sqrt{ee}\right) \times \left(1 + \frac{D}{2}\right)$$

Now $cde = \sqrt{ccddee}$ so that if this value is substracted from the value of (cde + cDe) we obtain the value of cDe, and the values thus obtained may be adjusted to give the corrected value obtained from Berstein's equation. The corrected value of cde can then be used to obtain the values of Cde and cdE from the ~~questions~~ equations

$$Cde = \sqrt{Cddee + (cde)^2} - cde$$
$$cdE = \sqrt{ccddE + (cde)^2} - cde$$

and the values thus obtained may be used to obtain the values for CDe and cDE by subtraction. (Calculations from Mourant, 1954)

The Australian figures for the phenotype distribution frequency (Simmons et al. 1944) for the white population based on tests of 350 persons are as follows:

Phenotype	%
CDE	16.57
CDee	54.00
CddE	0.00
Cddee	0.86
ccDE	12.57
ccDee	0.57
ccddE	0.57
ccddee	14.86

From these figures the chromosome distribution frequencies can be calculated, as indicated above, with the following results:

CDe	44.95
cde	37.20
cDE	15.24
Cde	1.13
cdE	0.76
cDe	0.71

Further from these figures the gene frequencies can be obtained by simple addition to give the following values:

C = 46.08	c = 53.91
D = 60.90	d = 39.09
E = 16.00	e = 83.99

The next level of testing is that which involves testing with four antisera, that is to say with anti-c in addition to the three used at the previous level. Twelve phenotypes become recognisable at this level of testing which, as related to their respective genotypes are set out in the following table. (See page 104)

The calculation of the chromosome distribution frequencies becomes a matter of some complexity, and the actual calculations need not be given here. The results obtained for the white Australian population (Simmons et al. 1946) based on tests of 225 individuals are as follows:

Genotype	Reaction with anti-			
	C	c	D	E
CDe/cDE CDe/cdE cDE/Cde cDE/CDE cDE/CdE cDe/CDE cDe/CdE CDE/cdE CDE/cde	+	+	+	+
CDe/CDE CDe/CdE CDE/CDE CDE/Cde CDE/CdE	+	-	+	+
CdE/cde CdE/cdE Cde/cdE	+	+	-	+
Cde/CdE CdE/CdE	+	-	-	+
CDe/cDe CDe/cde cDe/Cde	+	+	+	-
CDe/CDe CDe/Cde	+	-	+	-
cDE/cDE cDE/cDe cDE/cdE cDE/cde cDe/cdE	-	+	+	+
cdE/cdE cdE/cde	-	+	-	+
cDe/cDe cDe/cde	-	+	+	-
Cde/Cde	+	-	-	-
Cde/cde	+	+	-	-
cde/cde	-	+	-	-

CCDE	0.00
CCDee	23.56
CCddE	0.00
CCddee	0.44
CcDE	16.44
CcDee	31.56
CcddE	0.00
Ccddee	0.44
ccDE	12.44
ccDee	0.00
ccddE	0.44
ccddee	14.67

From these figures the following values for the chromosome distribution frequency can be obtained:

CDE	0.00
CDe	47.60
CdE	0.00
Cde	0.62
cDE	15.32
cdE	0.61
cDe	0.00
cde	35.84

and the corresponding gene distribution frequency figures are therefore:

C	=	48.12	c	=	51.77
D	=	62.92	d	=	37.07
E	=	15.93	e	=	84.06

The English figures, at this level of testing, are available and since they are based on tests on a much larger number of individuals than the corresponding Australian figures, they are cited here by way of comparison.

Phenotype	Race & Sanger (1950)	Fisher & Race (1946)	Murray (1946)
CCDE	0.00	0.11	0.10
CCDee	16.88	19.74	20.71
CCddE	0.00	0.00	0.00
CCddee	0.00	0.00	0.00
CcDE	12.99	13.59	11.46
CcDee	35.71	35.16	34.10
CcddE	0.00	0.00	0.00
Ccddee	0.65	0.65	0.58
ccDE	18.18	12.19	14.74
ccDee	0.65	2.48	2.31
ccddE	1.30	1.29	0.67
ccddee	13.64	14.78	15.32

By way of further comparison the corresponding figures for the Australian aboriginal population (Simmons et al. 1948) may be quoted. The phenotype frequency distribution figures are as follows, based on tests of 234 individuals.

CCDE ——— 2.99
CCDee ——— 47.86
CCddE ——— 0.00
CCddee ——— 1.71
CcDE ——— 27.35
CcDee ——— 10.26
CcddE ——— 0.00
Ccddee ——— 0.00
ccDE ——— 8.55
ccDee ——— 1.28
ccddE ——— 0.00
ccddee ——— 0.00

The corresponding chromosome frequency distribution figures for the aboriginal population may therefore be calculated to give the following values;

CDE ——— 2.08
CDe ——— 56.42
CdE ——— 0.00
Cde ——— 12.87
cDE ——— 20.09
cdE ——— 0.00
cDe ——— 8.54
cde ——— 0.00

and the gene distribution figures are therefore:

C	=	71.37	c	=	28.63
D	=	87.13	d	=	12.87
E	=	22.17	e	=	77.83

There is little point in continuing to repeat results obtained at all levels of testing. It will be sufficient to note that testing with five antisera, that is to say with anti-e in addition to the four already considered, eighteen phenotypes become distinguishable; the position being shown on the following table. (See page 108)

It may perhaps be added that when and if testing with anti-d becomes common it will then be possible to distinguish 27 phenotypes from among the 36 genotype combinations, but until an anti-d serum is unequivocally demonstrated testing must be confined to the five available antisera.

Genotype	Frequency in population	reactions with anti-				
		C	D	E	c	e
CDe/cDE CDe/cdE cDE/Cde cDe/CDE cDe/CdE CDE/cde	11.8648 0.9992 0.2775 0.0125 0.0000 0.1893	+	+	+	+	+
cDE/CDE cDE/CdE CDE/cdE	0.0687 0.0000 0.0058	+	+	+	+	-
CDe/CDE CDe/CdE CDE/Cde	0.2047 0.0000 0.0048	+	+	+	-	+
CDE/CDE CDE/CdE	0.0006 0.0000	+	+	+	-	-
CdE/cde Cde/cdE	0.0000 0.0234	+	-	+	+	+
CdE/cdE	0.0000	+	-	+	+	-
Cde/CdE	0.0000	+	-	+	-	+
CdE/CdE	0.0000	+	-	+	-	-
CDe/cDe CDe/cde cDe/Cde	2.1586 32.6808 0.0505	+	+	-	+	+
CDe/CDe CDe/Cde	17.6803 0.8270	+	+	-	-	+
cDE/cDe cDE/cde cDe/cdE	0.7243 10.9657 0.0610	-	+	+	+	+
cDE/cDE cDE/cdE	1.9906 0.3353	-	+	+	+	-
cdE/cdE	0.0141	-	-	+	+	-
cdE/cde	0.9235	-	-	+	+	+
cDe/cDe cDe/cde	0.0659 1.9950	-	+	-	+	+
Cde/Cde	0.0097	+	-	-	-	+
Cde/cde	0.7644	+	-	-	+	+
cde/cde	15.1020	-	-	-	+	+

FURTHER DEVELOPMENTS IN THE RH SYSTEM

Developments in the Rh system since 1944 have taken the form of discoveries of further allelomorphs at the three originally identified genetic loci and of discoveries of possible new loci within the same system. We will deal first with the new allelomorphs.

The first additional allelomorph to be discovered was reported in 1946 by Callender and Race. The antigen was christened C^W and is best known of the additional allelomorphs within the Rh system. The existence of this allele increases the number of possible chromosomes to twelve, the four additional chromosomes being;

C^WDe

C^Wde

C^WDE

C^WdE

of these the last three are of extremely low frequency, even C^WDe only has a distribution frequency of 0.0129, so that the gene frequency itself is also 0.0129. However, considering the twelve possible chromosomes, the number of possible genotypes within the Rh system is raised to 78, but in view of the great rarity of most of the additional genotypes it is hardly worth while setting out a complete analysis of the position here.

Further, but lesser known alleles at the C,c locus are C^X, C^u and c^v. The first was reported by Stratton and Renton (1954) and its rarity can be gathered from the fact that only four examples were found in tests on

3,931 unrelated individuals. Both C^u and c^v were reported by Race et al. (1948). The frequencies of neither antigen are known but since one example of each has been found in tests on 284 individuals, it may be that they are not quite so rare as C^w.

A further allele, D^u, at the D locus was reported by Stratton in 1946. It appears that D^u exists in several varieties, although more recent work seems to indicate that the so-called "high grade D^u" is not in fact due to the antigen D^u but rather to a position effect exerted by the chromosome Cde on the normal D antigen when the D gene is carried by the opposite chromosome.

Recent work indicates that there may be further alleles at the D locus but insufficient information is available at the moment to make it worth while to discuss this matter further here.

A further allele at the E locus, E^w, was reported by Greenwalt and Sanger in 1955. It appears to be a rare antigen only one example having been found so far. Another allele, E^u, was described by Ceppellini et al. (1950) whilst a possible e^x was described by Gilbey (1950). Again insufficient information is available to make it profitable to discuss the alleles further at this stage.

That appears to complete the list of allelomorphs existing at the CDE loci but yet further development in the Rh system has concerned the identification of additional loci. The first of these was reported by Rosenfield et al. (1953). The antigen which was recognised by the antibody which had been discovered was christened (f). On the assumption that absence of (f) indicated the presence of an allelomorph, the absence of (f) was indicated by F, although no anti-F has yet been

found.

A fifth locus of the Rh system was suggested by DeNatale et al. (1955) to account for a further antigen first reported by them. The exact status of this antigen is still in doubt and it has been provisionally christened V. It is possible however that V is an allele of (f). A further possibility is that V is the same as the recently reported G (Allen 1957).

Race and Sanger point out that, taking into account all the known alleles of the Rh system there are theoretically 288 different chromosome combinations giving rise to about 42,000 different Rh genotypes. In actual practice, however, the position is not quite so complex for, taking the European figures, 98% of all European chromosomes fall within one or other of the following combinations:

CdeFv
cdefv
cDEFv
cDefv
C^{W}DeFv
CdeFv
cdEFv
CD^{u}eFv

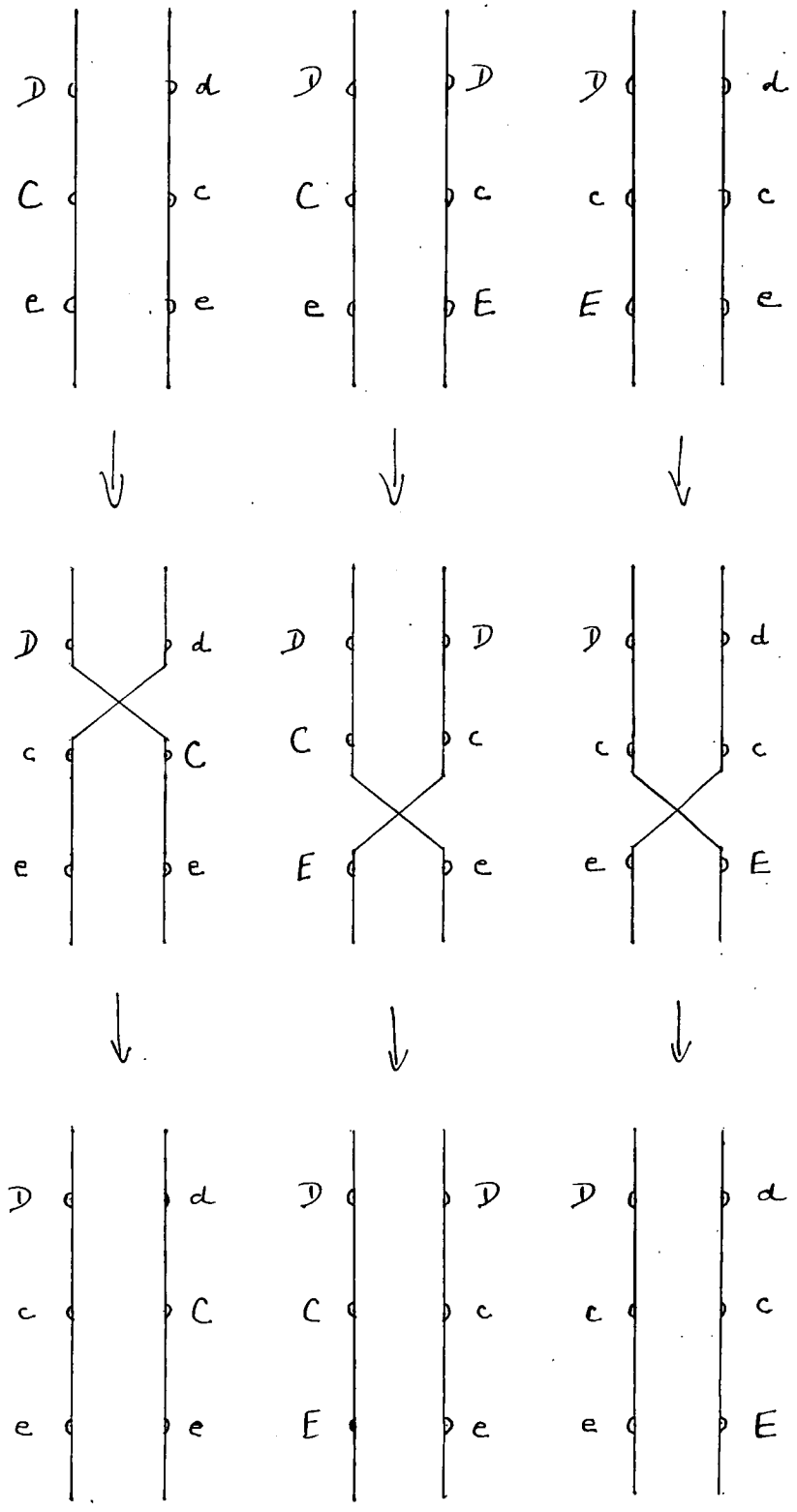
whilst the first three chromosomes of the above list account for 91% of all European genotypes.

A final complication of the Rh system which calls for a brief mention is the discovery of the existence of "deletion chromosomes". These are chromosomes in which there is an apparent lack of any gene at one or more of the genetic loci. The first of these to be reported (Race et al. 1950) was described as -D- the blood of persons concerned showing a total lack of all C and E allelomorphs. More recently two other examples displaying this phenomena have been reported. The first of these (Wiener et al. 1952)

is described, in the Fisher-Race nomenclature, as cD-; the second (Gunson and Donohue 1958) is described as $C^{W}D-$. As yet the "deletion" explanation appears only to be tentative, but it is mentioned here since the same phenomenon is also encountered in other blood group systems, and in connection with some of these alternative explanations have, in some cases, been offered which may well apply also in the case of the Rh system. These will be more fully discussed later.

One final matter to which reference may be made is the phenomenon of crossing-over. This is a matter to which we referred in the Introduction and in Fisher's theory we see the possibility that crossing-over has in fact taken place. Fisher was concerned to account for the very low frequency of some of the chromosome combinations and he has suggested that the genes of the Rh system are not absolutely linked so that cross-overs can occasionally occur; the rare gene combinations resulting from cross-overs from the commoner. He has further suggested that the actual order of genes on the chromosome is not CDE but rather DCE.

Thus taking the three commonest European chromosomes CDe, cde and cDE Fisher has shown that the less common combinations cDe, cdE and CDE can be explained as resulting from cross-overs between the three common combinations as follows:


D d
C c
e e
D D
C c
e E
D d
c c
E e
D d
c C
e e
D D
C c
E e
D d
c c
e E
D d
c C
e e
D D
C c
E e
D d
c c
e E

Since crossing-over in such a way as to separate the three loci of the Rh system would be a fairly rare event the rarity of some of the gene combinations would be explained. The same explanation would also account for the extremely rare chromosome CdE. This could not result from a crossing between the three common chromosomes but only as the result of a further crossing involving one of the second order chromosomes such as a cross between cDE and dCe. Since the second order chromosome itself is rare a further crossing involving such a chromosome would be rare indeed and would explain the extremely low frequency of CdE.

INHERITANCE OF THE RH SYSTEM

Following Race and Sanger we will discuss the inheritance of the individual antigens before discussing the inheritance of the system as a whole.

Inheritance of D: That D is inherited as a Mendelian dominant characteristic is established by the family data which in terms of the fundamental phenotypes Rh+ and Rh- is as follows:

Matings			Children			
			Rh+		Rh-	
Type	obs.	exp.	obs.	exp.	obs.	exp.
Rh+ x Rh+	42	42.936	151	145.5	7	12.5
Rh+ x Rh-	12	15.636	37	34.5	11	13.5
Rh- x Rh-	6	1.422	0	0.0	31	31.0
Total	60	59.994	188	180.0	49	57.0

Source: Landsteiner & Wiener 1941

This shows a reasonably good fit and the result is supported by the published results of 57 Rh- x Rh- matings producing 131 offspring only one of which was Rh- (and this was shown to be extra marital by the MN groups). (Race & Sanger 1958)

Inheritance of E and e: The inheritance of E and e as Mendelian alleles is shown by the usual family data information which is tabulated below:

Matings		Children					
		EE		Ee		ee	
Type	No.	obs.	exp.	obs.	exp.	obs.	exp.
EE x EE	0	0	0.00	—	—	—	—
EE x Ee	11	13	12.00	11	12.00	—	—
EE x ee	17	—	—	37	37.00	—	—
Ee x Ee	32	18	18.25	41	36.00	14	18.25
Ee x ee	163	—	—	200	193.50	187	193.50
ee x ee	239	—	—	1	—	556	557.00

Source: Race and Sanger (1958)

These results show a very satisfactory fit and they are supported by the published results of 592 ee x ee matings 1,031 children of which only three were E positive and of these two were shown to be extra marital, one by the ABO system and one by the MN system.

Inheritance of C and c: Once again we see that the inheritance follows the normal pattern of the Rh system, the family data being as follows:

Matings		CHILDREN					
		CC		Cc		cc	
Type	No.	obs.	exp.	obs.	exp.	obs.	exp.
CC x CC	42	84	84.00	—	—	—	—
CC x Cc	189	185	193.00	201	193.00	—	—
CC x cc	240	—	—	449	450.00	(1)	—
Cc x Cc	241	119	123.75	260	247.50	116	123.75
Cc x cc	451	—	—	432	409.00	386	409.00
cc x cc	204	—	—	—	—	400	400.00
Total	1367	388	400.75	1342	1299.00	903	932.75

Source: Race and Sanger (1958)

Inheritance of the Rh system: The same principles govern the inheritance of a chromosome with its gene complement as govern the inheritance of a single gene, assuming, of course, that no crossing-over occurs: indeed as we saw when discussing the fundamental principles of genetics it is actually the chromosomes which segregate rather than the individual genes. Thus no child can possess a genetic combination of genes which is not carried by either of its parents. Thus instead of speaking of the inheritance of C or D or E one speaks of the inheritance of CDe, cde or cDE. If we therefore consider a mating of the type CDe/cde x CDE/cDe it can be seen that the issue must be one of the following genotypes:

CDe/cDE
CDe/cDe
cde/cDE
cde/cDe

A full analysis of all possible genotype matings and their offspring with relevant frequencies is a rather complex matter much depending upon the level at which the testing is undertaken and the number, therefore, of recognisable phenotypes. Little would be achieved by attempting such an analysis at this stage, but a partial analysis will be attempted when the problems of paternity are discussed at a later stage.

DEVELOPMENT OF THE Rh ANTIGENS

As is the case with most antigens the Rh antigens appear to be well developed before birth. Bornstein and Israel (1942) found D to be present in a number of foetuses the youngest of which was only 17 cms,, which, assuming this measurement to be the crown-rump length, would mean that the foetus was approximately four months old. (If the measurement was the crown-heel length the age would be approximately three months.)

Mollison and Cutbush (1949) have found C, c and D well developed as early as fourteen weeks, whilst Chown (1955) appears to hold the record with the detection of Rh antigens in a foetus of six weeks.

THE LUTHERAN BLOOD GROUP SYSTEM

The existence of an antibody defining the Lutheran system was first reported by Callender et al. (1945). The independence of the system from the ABO, MN, P and Rh systems was demonstrated by Callender and Race (1946).

The gene responsible for the antigen that was stimulating the antibody was denoted by Lu^a (originally L); the antibody was therefore denoted by anti-Lu^a and the phenotypes that it was capable of distinguishing were denoted by Lu(a+) and Lu(a-).

The existence of a gene allelic to Lu^a was postulated, but until the discovery of the anti-body anti-Lu^b ten years later (Cutbush and Chanarin 1956) it could only be recognised by the absence of Lu^a.

The existence of two allelic genes underlying the Lutheran system means that three genotypes are possible, but until anti-Lu^b becomes more widely available it is only possible, using anti-Lu^a, to distinguish between two phenotypes which are related to the three possible genotypes as follows:

Genotype	Phenotype
Lu^aLu^a, Lu^aLu^b	Lu(a+)
Lu^bLu^b	Lu(a-)

The distribution frequency for the two phenotypes shows the usual racial variation. The Australian figures (Simmons et al. 1953) for the white population, based on tests upon 100 individuals are as follows:

Lu(a-) 93%
Lu(a+) 7%

The corresponding figures for the aboriginal population, based on tests on 178 individuals (Sanger et al. 1951) are as follows:

Lu(a-) 100%
Lu(a+) 0%

The figures for the British Isles, based on 2,539 tests may be quoted by way of comparison. They are as follows:

Investigation	Population	No.	Phenotype %	
			Lu(a+)	Lu(a-)
Callender et al.(1946)	English	582	7.90	92.10
Mainwaring et al.(1948)	"	316	8.23	91.77
Bertinshaw et al.(1950)	"	475	6.95	93.05
Ikin et al.(1952)	"	1166	6.09	93.91
"	Welsh	116	0.86	99.14
"	Scottish	527	5.50	94.50
"	Irish(N.I.)	106	8.49	91.51

From the phenotype frequency distribution figures the gene frequencies can be calculated as follows:

$$Lu^b = \sqrt{Lu(a-)}$$

$$Lu^a = 1 - \sqrt{Lu(a-)}$$

Using the Australian figures, therefore, the gene frequency distribution figures will be -

Lu^b 0.9644

Lu^a 0.0356

From these results the genotype frequencies can be calculated in the usual way, with the following results:

$Lu^bLu^b = (0.9644)^2 = 0.9303$
$Lu^aLu^a = (0.0356)^2 = 0.0012$
$Lu^aLu^b = (2 \times 0.0356 \times 0.9644) = 0.0686$

No population figures are yet available in which tests with both anti-Lu^a and anti-Lu^b have been carried out so that no check is available on the calculated genotype frequencies. However one test (Cutbush and Chanarin 1956) on a random sample of 532 persons with anti-Lu^b revealed that they were all positive which is at least consistent with the calculated rarity of Lu^a.

Although the work of Mainwaring and Pickles (1948) indicated that, using anti-Lu^a, it was possible to distinguish between strongly and weakly reacting Lu(a+) cells the suggested possibility that there exist sub-groups within the Lutheran system analogous to the A_1 and A_2 groups in the ABO system is negatived by the more recent work of Race and Sanger (1958) who showed that the variability in the strength of the Lu^a antigen follows a normal distribution curve and does not, therefore, reflect the existence of additional alleles, although the strength of the antigen may, at least partially, be genetically determined.

INHERITANCE OF THE LUTHERAN SYSTEM

It was established by Callender and Race (1946) that Lu^a was inherited as a Mendelian dominant. This is clearly borne out by the family data available. If we consider the system as defined by anti-Lu^a there are three different mating types to be considered. These, with their possible offspring are shown in the following table:

Matings		Proportion of Children	
Type	Frequency	Lu(a+)	Lu(a-)
Lu(a+) x Lu(a+)	0.0058	0.7586	0.2414
Lu(a+) x Lu(a-)	0.1413	0.5099	0.4901
Lu(a-) x Lu(a-)	0.8529	0.0000	1.0000

The published data is summarised in the following table:

Matings				Lu(a+)		Lu(a-)	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
Lu(a+) x Lu(a+)	5	2.145	12	10	9.212	2	2.897
Lu(a+) x Lu(a-)	63	57.03	118	64	60.17	54	57.83
Lu(a-) x Lu(a-)	370	378.8	859	0	0.00	859	859.00
Total	438	437.975	989	74	69.382	915	919.727

Sources: Mainwaring & Pickles (1948)
Lawler (1950)
Race et al. (1953)
Race et al. (1957)

This shows a satisfactory fit.

If anti-Lu^b is used then there are six matings to be considered and these with their possible offspring are shown in the following table. Since there are no published family studies involving testing with anti-Lu^b there is no check on the calculated frequencies.

Matings		Children		
Type	Frequency	Lu^aLu^a	Lu^aLu^b	Lu^bLu^b
$Lu^aLu^a \times Lu^aLu^a$	0.0000	0.0000	- -	- -
$Lu^aLu^a \times Lu^aLu^b$	0.0002	0.0001	0.0001	- -
$Lu^aLu^b \times Lu^aLu^b$	0.0056	0.0014	0.0028	0.0014
$Lu^aLu^a \times Lu^bLu^b$	0.0028	- -	0.0028	- -
$Lu^aLu^b \times Lu^bLu^b$	0.1385	- -	0.06925	0.06925
$Lu^bLu^b \times Lu^bLu^b$	0.8529	- -	- -	0.8529

DEVELOPMENT OF THE LUTHERAN ANTIGENS

Race and Sanger (1958) found that the Lu^a antigen was well developed in a twelve weeks old foetus and demonstrated that this could not have been due to placental transfusion since the foetus was Lu(a-) whilst the mother was Lu(a+). There appears to be no published information on the development of the Lu^b antigen.

LINKAGE

The Lutheran system is the first of the blood group systems to reveal evidence of linkage. Mohr (1951) published results which were strong evidence of linkage between the Lutheran and Lewis systems, this being the first reported example of autosomal linkage in man. Although the existence of linkage is also supported by the work of Race and Sanger (1958) the latter suggest that the linkage is not between the Lutheran and Lewis genes, but between the Lutheran genes and the secretor genes associated with the Lewis system.

This matter will be more fully discussed when the Lewis system is considered.

THE KELL BLOOD GROUP SYSTEM

The Kell blood group system was first discovered by Coombs et al.(1946) as an immediate result of the introduction of the Coombs anti-human globulin test which demonstrated a "new" incomplete antibody. The antigen which was recognised by the antibody was called K, the antibody itself being named anti-K. A second example of this antibody was found by Wiener and Sonn-Gordon (1947) which, because it was not immediately identified as anti-K was called Si.

The antibody corresponding to the expected allele of K, anti-k was first reported by Levine et al.(1949) but again, since its relationship to the Kell system was not immediately appreciated, it was originally named anti-Cellano.

Considering the system as defined by anti-K, two phenotypes can be recognised K+ and K-. The existence of the allele k, however, means that there must be three genotypes which will be related to the two distinguishable phenotypes as follows:

Genotype	Phenotype
kk	K-
Kk) KK)	K+

The Australian figures for the distribution frequency of the two phenotypes (Simmons et al. 1953) based on tests on 100 individuals from the white population are as follows:

K+ 9%

K- 91%

There appear to be no published figures for the aboriginal population, but the results obtained on related races suggest that tests would reveal a complete absence of K.

The corresponding English figures which may be quoted by way of comparison are as follows:

Investigation	No. tested	K+		K-	
		No.	%	No.	%
Dunsford (1949)	566	41	7.26	525	92.74
Sanger et al.(1949)	423	43	10.17	380	89.83
Bertinshaw et al.(1950)	475	33	6.95	442	93.05
	1464	117	8.00	1347	92.00

Using the Australian figures, quoted above, the gene frequencies can be calculated in the usual way:

$$K = \sqrt{0.9100} = 0.9539$$

$$k = 1 - \sqrt{0.9100} = 0.0461$$

From these figures the genotype frequencies can be obtained as follows:

$$KK = (0.0461)^2 = 0.0021$$

$$Kk = 2(0.0461 \times 0.9539) = 0.0879$$

$$kk = (0.9539)^2 = 0.9100$$

Since no tests have been made in Australia using both anit-K and anti-k no check is available for these figures, but a check is available in the case of the English figures. Thus the results obtained by Ikin et al. (1952) using both anti-K and anti-k may be compared with the calculated frequencies obtained by Race and Sanger (1958) from tests on 1,108 persons using only anti-K: the results of Ikin et al. were obtained from tests on 1,166 persons:

Genotype	Ikin	Race & Sanger
KK	0.09	0.0021
Kk	0.0763	0.0872
kk	0.9228	0.9107

It may be added that using both anti-K and anti-k the results may be tabulated in a slightly different form, namely,

K+k-
K+k+
K-k+

Considered in this form it can be seen that there is, theoretically, the possibility of yet a further genotype, namely, K-k-. In fact such a genotype has been reported (Chown et al. 1957) but it is obviously extremely rare for although the tests of Levine et al. and those of Lewis et al. would have detected such a genotype no example was in fact found although their combined work involved tests on 5,372 individuals.

The K-k- genotype has not yet been explained. It comes within the same general category as the "deletion" chromosomes of the Rh system, but the current explanation of the K-k- type appears to be the suggestion that there may exist a third rare allele at the Kell locus whose antibody has yet to be discovered.

FURTHER DEVELOPMENTS IN THE KELL BLOOD GROUP SYSTEM

The discovery that the Kell system, like most of the others, was more complex than it at first appeared was made by Allen (1956) who reported the existence of two new antibodies which have been christened anti-Kp^a and anti-Kp^b and have even suggested the possibility of a third antibody anti-Kp^c. Allen's original suggestion as to the relationship of these antibodies to the Kell system was that Kp^a and Kp^b are related to K and k in the same way in which E and e are related to C and c in the Rh system. Race and Sanger (1958), however, put forward the possibility that Kp^a is an allele of K and k whilst anti-Kp^b is really anti-Kk. At the moment it appears not possible to say very much more regarding these new antibodies. So far as their frequency goes it may be added that anti-Kp^a sensitised the cells of 51 out of 2,363 individuals whilst Kp^b sensitised the cells of all but one of 2,363 individuals.

It may finally be added that a further complication results from the fact that the individual who was found to be K-k- was also found to be Kp(a-b-). The antibody carried by this individual is of, as yet, unknown specificity.

INHERITANCE OF THE KELL SYSTEM

It was soon established that the K gene is inherited as a Mendelian dominant characteristic. This is established by the usual family data test. Considering the Kell system as defined by anti-K it can easily be seen that there are three different mating types to be considered. These with their offspring are tabulated below:

Matings		Children	
Type	Frequency	K+	K-
K+ x K+	0.0080	0.7625	0.2375
K+ x K-	0.1626	0.5117	0.4883
K- x K-	0.8294	—	1.0000

The published family data, which is set out below, shows a good fit with the calculated frequencies.

			CHILDREN				
	Matings			K+		K-	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
K+ x K+	7	3.68	16	11	12.20	5	3.80
K+ x K-	74	74.80	179	88	91.59	91	87.41
K- x K-	379	381.52	827	0	0.00	827	827.00
	460		1102	99		923	

The theory is also confirmed by the evidence of the results of K- x K- matings. Race and Sanger (1958) report the results of tests on K- x K- matings producing 1,262 children all of which were K-.

The position where anti-k is used as well as anti-K becomes, as usual, slightly more complex. The calculated frequencies are tabulated below, but there are no published results with which to compare them.

Matings		Children		
Type	Frequency	KK	Kk	kk
KK x KK	0.0000	0.0000	—	—
KK x Kk	0.0004	0.0002	0.0002	—
Kk x Kk	0.0076	0.0019	0.0038	0.0019
KK x kk	0.0038	—	0.0038	—
Kk x kk	0.1583	—	0.0794	0.0794
kk x kk	0.8294	—	—	0.8294

DEVELOPMENT OF THE KELL ANTIGENS

The Kell antigens, both K and k, are well developed at birth. Race and Sanger (1958) observe that since anti-K is a potent cause of haemolytic disease the antigens are presumably well developed early in uterine life, but there appear to be no published observations on the point as yet.

THE KIDD BLOOD GROUP SYSTEM

The Kidd blood group system was discovered by Allen et al.(1951) when they found a "new" antibody in the serum of a woman suffering from haemolytic disease of the newborn (erythroblastosis foetalis). The antigen responsible was christened Jk^a and the antibody, therefore, anti-Jk^a. The antibody corresponding to the expected allele Jk^b was first identified in 1953 by Plaut et al.

With two allelic genes three genotypes are possible, but testing with anti-Jk^a alone only two phenotypes are distinguishable which are related to their genotypes as follows:

Jk^aJk^a, Jk^aJk^b ..... Jk(a-)

Jk^bJk^b ..... Jk(a-)

We have been able to find no published figures relating to the frequency distribution of the phenotypes in Australia, but the English figures which rarely, in other cases, differ very much from the Australian figures relating to the white population are as follows:

Investigation	Total	Phenotype %	
		Jk(a-)	Jk(a-)
Race et al.(1951)	201	76.62	23.38
Sanger et al.(1953)	343	73.76	26.24

The gene frequency figures can be obtained from these results in the usual way. The figures we propose to quote, however, are those calculated by Race and Sanger (1958) based on tests on 4,275 Caucasians. The results were as follows:

$$Jk^b = \sqrt{0.2360} = 0.4858$$

$$Jk^a = 1 - \sqrt{0.2360} = 0.5142$$

From these figures the genotype frequencies will be

$$Jk^aJk^a = (0.5142)^2 = 0.2644$$

$$Jk^aJk^b = 2(0.5142 \times 0.5142) = 0.4996$$

$$Jk^bJk^b = (0.4858)^2 = 0.2360$$

These calculated results are borne out by the result of testing with both anti-Jk^a and anti-Jk^b. The results of such tests, quoted from Race and Sanger, are as follows:

Jk(a+b-).....0.2727
Jk(a+b+).....0.5055
Jk(a-b+).....0.2218

It may be added that no example of Jk(a-b-) has yet been found.

INHERITANCE OF THE KIDD SYSTEM

That Jk^a follows the normal pattern of inheritance as a Mendelian dominant was established by Race et al.(1951). This is clearly supported by the family data. Taking the Kidd system as defined by anti-Jk^a it can be seen that there are three mating types to be considered. These with their offspring are tabulated below:

Matings		Children	
Type	Frequency	Jk(a+)	Jk(a-)
Jk(a+) x Jk(a+)	0.5837	0.8931	0.1069
Jk(a+) x Jk(a-)	0.3606	0.6730	0.3270
Jk(a-) x Jk(a-)	0.0557	0.0000	1.0000

These calculated frequencies may be compared with the observed results which are as follows:

Matings			Children				
				Jk(a+)		Jk(a-)	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
Jk(a+) x Jk(a+)	66	65.50	152	134	135.04	18	16.96
Jk(a+) x Jk(a-)	39	44.09	78	51	51.94	27	26.06
Jk(a-) x Jk(a-)	12	7.42	25	(1)	0.00	24	25.00
	117	117.01	235	186	186.98	69	68.02

Source: Race and Sanger (1954)

Where the testing is done with both anti-Jk^a and anti-Jk^b there will be six mating types to be considered and these with their offspring are tabulated below:

Matings		Children		
Type	Frequency	Jk^aJk^a	Jk^aJk^b	Jk^bJk^b
Jk^aJk^a x Jk^aJk^a	0.0699	0.0699	—	—
Jk^aJk^a x Jk^aJk^b	0.2642	0.1321	0.1321	—
Jk^aJk^b x Jk^aJk^b	0.2496	0.0624	0.1248	0.0624
Jk^aJk^a x Jk^bJk^b	0.1248	—	0.1248	—
Jk^aJk^b x Jk^bJk^b	0.2358	—	0.1179	0.1179
Jk^bJk^b x Jk^bJk^b	0.0557	—	—	0.0557

There appears to be only one published series of figures with which the above series of calculated results may be compared. These are the figures quoted by Race and Sanger (1958) which are as follows:

Matings				Children					
				Jk^aJk^a		Jk^aJk^b		Jk^bJk^b	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.	obs.	exp.
Jk^aJk^axJk^aJk^a	3	4.7	6	6	6.00	0	0.00	0	0.00
Jk^aJk^axJk^aJk^b	16	17.7	39	15	19.50	24	19.50	0.	0.00
Jk^aJk^bxJk^aJk^b	21	16.7	54	14	13.50	27	27.00	13	13.50
Jk^aJk^axJk^bJk^b	9	8.4	16	0.	0.00	16	16.00	0	0.00
Jk^aJk^bxJk^bJk^b	14	15.8	26	0.	0.00	21	13.00	5	13.00
Jk^bJk^bxJk^bJk^b	4	3.9	7	0	0.00	0	0.00	7	7.00
Total	67	67.2	148	35	39.00	88	75.50	25	33.00

It will be noted that there is a good fit save with regard to the distribution of the offspring of the Jk^aJk^b x Jk^bJk^b mating. It should be emphasised, however, that the sample is rather small - with further testing on larger numbers it is probable that a more normal distribution will be found.

THE DEVELOPMENT OF THE KIDD ANTIGENS

Race and Sanger (1953) report that Jk^a was found to be well developed in a seventeen week old foetus. There are apparently no published observations on the development of Jk^b in foetal blood, but antigens appear to be well developed in cord blood.

THE DUFFY BLOOD GROUP SYSTEM

The existence of the Duffy blood group system was first reported by Cutbush et al.(1950). The antigen responsible for the antibody that was then discovered was christened Fy^a, the antibody, therefore, being anti-Fy^a. The expected allelomorph Fy^b was identified in 1951 by Ikin et al. with the discovery of anti-Fy^b.

With two alleles we have as usual three possible genotypes, whilst on testing with anti-Fy^a alone two phenotypes are distinguishable which are related to the genotypes as follows:

$$\left.\begin{matrix} Fy^aFy^a \\ Fy^aFy^b \end{matrix}\right\} \ldots\ldots\ldots\ldots\ Fy(a+)$$

$$Fy^bFy^b \ldots\ldots\ldots\ldots\ Fy(a-)$$

The Australian figures for the frequency distribution of the two recognisable phenotypes (Simmons et al. 1953) based on tests of 100 individuals are as follows:

$$Fy(a+) \ldots\ldots\ldots\ 70\%$$

$$Fy(a-) \ldots\ldots\ldots\ 30\%$$

The corresponding English figures, based on tests of 2201 individuals show a similar distribution. They are tabulated below:

Investigation	No.	Fy(a+)		Fy(a-)	
		No.	%	No.	%
Cutbush & Mollison (1950)	205	133	64.88	72	35.12
Race et al.(1951)	255	167	65.49	88	34.51
Race & Sanger (1952)	325	218	67.08	107	32.92
Race et al.(1953)	250	162	64.80	88	35.20
Ikin et al.(1952)	1166	764	65.52	402	34.48
Totals	2201	1444	65.55	757	34.45

Using the Australian figures the gene frequencies may be calculated in the usual way:

$$Fy^b = \sqrt{0.3000} = 0.5476$$

$$Fy^a = 1 - \sqrt{0.3000} = 0.4524$$

From these figures the genotype frequencies can be calculated as follows:

$$Fy^aFy^a = (0.4524)^2 = 0.2046$$

$$Fy^aFy^b = 2(0.5476 \times 0.4524) = 0.4954$$

$$Fy^bFy^b = (0.5476)^2 = 0.3000$$

Such limited testing as has been done using both anti-Fy^a and anti-Fy^b confirms these calculated distribution frequencies:

Genotype	obs.	exp.
Fy(a+b-)	31	25.9
Fy(a+b+)	70	73.3
Fy(a-b+)	50	51.8

As we have seen in the case of other groups, however, there is a fourth genotype possible under these circumstances, namely an Fy(a-b-) genotype and Sanger et al.(1955) found that this genotype was encountered in the majority of negroes. This has been explained by the hypothesis that there exists a third allele designated Fy for which no antibody has yet been discovered. This hypothesis receives support from the tests made on New York negroes by Sanger et al.(1955) the results of which are tabulated below:

Phenotype	Genotype	obs.	exp.
Fy(a+b-)	Fy^aFy^a Fy^aFy	11	11.4
Fy(a+b+)	Fy^aFy^b	2	1.6
Fy(a-b+)	Fy^bFy^b Fy^bFy	27	27.0
Fy(a-b-)	FyFy	85	85.0

From these figures the gene frequencies among New York negroes can be calculated to be:

Fy^a 0.0534

Fy^b 0.1220

Fy 0.3246

It may be added that Race and Sanger (1958) report that the frequency of the phenotype Fy(a-b-) is even higher among West African negroes than among those of New York. No example of Fy(a-b-) has yet been found in European blood.

INHERITANCE OF THE DUFFY BLOOD GROUP SYSTEM

It was early established that Fy^a is inherited as a Mendelian dominant characteristic. This can be established in the usual way by reference to family data studies. Taking the system as defined by anti-Fy^a there are the usual three mating types to be considered, and these with their expected offspring are tabulated below:

Matings		Children	
Type	Frequency	Fy(a+)	Fy(a-)
Fy(a+) x Fy(a+)	0.4317	0.8636	0.1364
Fy(a+) x Fy(a-)	0.4507	0.6307	0.3693
Fy(a-) x Fy(a-)	0.1176	0.0000	1.0000

The results obtained from a study of 391 English families with 864 children which may be compared with the above calculated results are tabulated below:

Sources: Cutbush & Mollison (1950)
Race, Holt & Thompson (1951)
Race & Sanger (1952)
Race, Sanger & Thompson (1953)
Race, Sanger & Moores (1957)

Matings			Children				
				Fy(a+)		Fy(a-)	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
Fy(a+) x Fy(a+)	152	168.9	334	287	288.4	47	45.54
Fy(a+) x Fy(a-)	185	176.2	408	255	257.3	153	150.9
Fy(a-) x Fy(a-)	54	45.98	122	0	0.0	122	122.00
Totals	391		864	542		322	

The fit can be seen to be very good. It will be noted that all the 122 children from the 54 Fy(a-) x Fy(a-) matings were Fy(a-) whilst in addition it may be noted that Race and Sanger (1958) refer to further tests by Ceppellini of 129 families with 434 children in which again all the issue of Fy(a-) x Fy(a-) matings were Fy(a-).

The situation where both anti-Fy^a and anti-Fy^b are used for testing is shown below. There are, however, no published results, as yet, of such tests and there are no observed results which can be compared with the calculated frequencies.

Matings		Children		
Type	Frequency	Fy^aFy^a	Fy^aFy^b	Fy^bFy^b
$Fy^aFy^a \times Fy^aFy^a$	0.0295	0.0295	—	—
$Fy^aFy^a \times Fy^aFy^b$	0.1167	0.03335	0.03335	—
$Fy^aFy^b \times Fy^aFy^b$	0.2355	0.058875	0.11775	0.058875
$Fy^aFy^a \times Fy^bFy^b$	0.1178	—	0.1178	—
$Fy^aFy^b \times Fy^bFy^b$	0.3329	—	0.16645	0.16645
$Fy^bFy^b \times Fy^bFy^b$	0.1176	—	—	0.1176

If the assumption is made that there is a third allele among negroes then clearly the above analysis of inheritance will not apply in populations in which such a third allele is found. With a third allele the number of genotypes is raised to six among which four phenotypes can be distinguished by means of anti-Fy^a and anti-Fy^b. This means that there will be ten phenotypically distinct mating types, with twenty-one genotypically distinct mating types. There is little point in setting out a full analysis of all these various matings at this stage. The point will be more fully considered when problems of disputed paternity are discussed.

THE DEVELOPMENT OF THE DUFFY ANTIGENS

Cutbush and Mollison (1950) found Fy^a to be well developed in a 17 week old foetus, but there appear to be no published observations on the development of Fy^b, nor of course for the still hypothetical Fy.

THE SECRETOR SYSTEM

Before discussing the Lewis blood group system, the last of the major blood group systems that we have to consider, it will be of assistance if we briefly glance at the secretor system, for the two are closely related. (Grubb, 1948).

The presence of ABO antigens in tissues other than the red cells has been known for some years, in particular their presence in saliva was first noted by Yamakami in 1926. In 1930 Lehrs and Putkonen discovered that the presence of the antigens in other body fluids and organs was not universal but was limited to persons, known as "secretors", secretion being a genetically determined phenomenon unrelated to the other ABO genes, and in 1932 the ability to secrete was shown by Schiff and Sasaki to be inherited as a Mendelian dominant. The gene responsible for secretion is designated Se, its allele being se.

Further work by Friedenreich and Hartmann suggests that there are two forms of the ABO antigens;

a) a water soluble form which is not present in red cells but is found in the body fluids and organs of "secretors"

b) an alcohol soluble form which is present in both red cells and other tissues but which is unaffected by the secretor genes.

It will be recalled that the Xx and Yy genes of the ABO system which act as inhibiting genes are also related to the secretion system. The following diagram, from Race and Sanger (1957) shows the way in which these various genes may be inter-related.

There seem to be few published figures relating to the frequency distribution of the secretor genes. Using the figures quoted by Race and Sanger (1958) the gene frequency figures for England are:

$$se = 0.4923$$

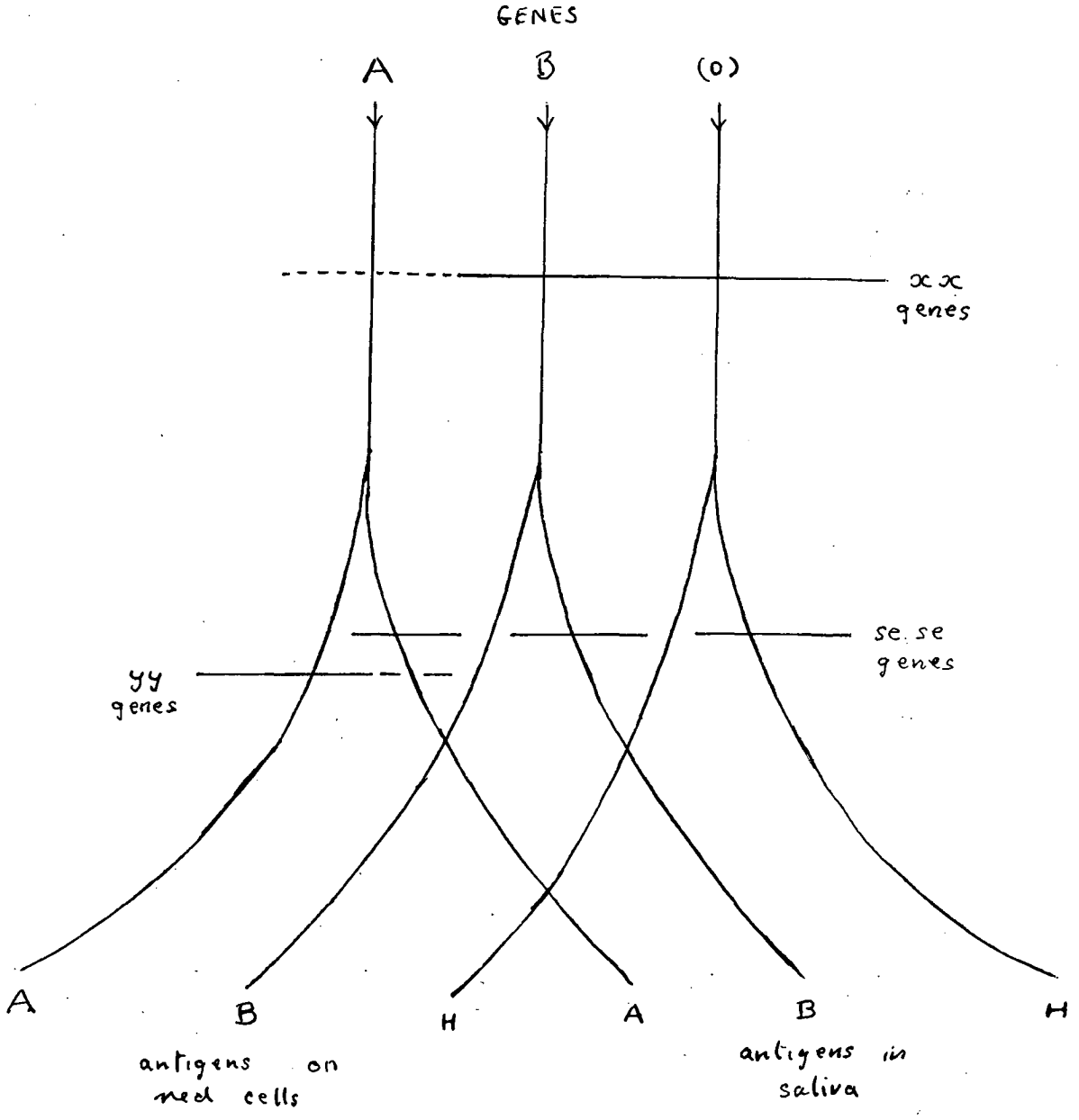
$$Se = 0.5077$$

Two such allelomorphs give rise to three genotypes and the genotype frequencies will therefore be:

$$SeSe = (0.5077)^2 = 0.2577$$

$$Sese = 2(0.5077 \times 0.4923) = 0.4999$$

$$sese = (0.4923)^2 = 0.2424$$


GENES
A
B
(O)
xx genes
se.se genes
yy genes
A
B
H
A
B
H
antigens on red cells
antigens in saliva

INHERITANCE OF THE SECRETION SYSTEM

The fact that Se is inherited as a Mendelian dominant can be established in the normal way by consideration of the family data. Two recognisable phenotypes give rise to three distinct mating types which, with the expected issue are tabulated below, using the symbols S+ to indicate a secretor and S- a non-secretor.

Matings		Children	
Type	Frequency	S+	S-
S+ x S+	0.5740	0.8911	0.1089
S+ x S-	0.3672	0.6699	0.3301
S- x S-	0.0588	0.0000	1.0000

If the observed results obtained by Race et al.(1949) and Andresen (1952) be added to those collected by Wiener (1943) the combined results may be tabulated as follows. It may be added that the results obtained by Moharram (1943) and Chown and Lewis (1955) have been omitted on the ground that they involve tests on non-European populations and reflect racial variations in frequency distribution. Thus that of Chown and Lewis, obtained from tests on the Blood Indians reveal a total absence of non-secretors.

	Matings		CHILDREN				
				S+		S-	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
S+ x S+	226	216.4	540	480	481.1	60	58.82
S+ x S-	123	138.5	327	211	219.1	116	107.9
S- x S-	28	22.15	70	0	0.0	70	70.0
Total	377		937	691		246	

With two allelomorphs there are of course six genotypically distinct matings, and these with their offspring are tabulated below. There are, however, no published results with which the calculated frequencies can be compared:

Matings		Children		
Type	Frequency	SeSe	Sese	sese
SeSe x SeSe	0.0664	0.0664	—	—
SeSe x Sese	0.2576	0.1288	0.1288	—
Sese x Sese	0.2500	0.0625	0.1250	0.0625
SeSe x sese	0.1248	—	0.1248	—
Sese x sese	0.2424	—	0.1212	0.1212
sese x sese	0.0588	—	—	0.0588

THE DEVELOPMENT OF THE SECRETION SYSTEM

Wiener and Belkin (1943) testing for groups other than group O found that the ability to secrete the ABH substances is well established at the time of birth, whilst Formaggio (1951) found that the saliva of the new-born neutralised "anti-O serum" to the same extent as saliva of group O adults.

THE LEWIS BLOOD GROUP SYSTEM

The Lewis system was discovered by Mourant (1946) when he reported the existence of a new antibody which appeared to be independent of the other known systems. The antigen responsible for the production of the antibody was christened Le^a and the antibody therefore anti-Le^a. The expected allele was identified in 1948 when Andresen reported the existence of anti-Le^b.

With two alleles the system, as defined by anti-Le^a can be set out in the usual form. The only modification necessary being that, as Andresen showed (1948) Le^a was probably recessive and not dominant. Thus the system may be set out as follows:

Le^aLe^a ..... Le(a+)

Le^aLe^b)
Le^bLe^b) ..... Le(a-)

The frequency distribution of these phenotypes shows the usual racial variation. The Australian figures (Simmons et al. 1950 - 1) are as follows:

Le(a-) 72.64%
Le(a+) 27.36%

The English figures, by way of comparison are as follows:

Investigation	Total	Le(a+)		Le(a-)	
		obs.	exp.	obs.	exp.
Mourant (1946)	96	24	25.00	72	75.00
Grubb 7 Morgan (1949)	212	47	22.17	165	77.83
Bertinshaw (1950)	475	106	23.32	369	77.68
Race et al. (1949)	571	127	22.17	444	77.83
Total	1354	304	22.46	1050	77.54

From the Australian figures the gene and genotype frequencies may be calculated in the usual way:

$$Le^a = \sqrt{0.2736} = 0.5230$$
$$Le^b = 1 - \sqrt{0.2736} = 0.4770$$

The corresponding genotype frequencies will therefore be

$$Le^aLe^a = (0.5230)^2 = 0.2736$$
$$Le^aLe^b = 2(0.5320 \times 0.4770) = 0.4989$$
$$Le^bLe^b = (0.4770)^2 = 0.2275$$

Consideration of the observed results of tests using both anti-Le^a and anti-Le^b gave rise to the first suggestion that the Lewis system did not follow the pattern of the earlier systems. In the first place Andresen found that his anti-Le^b gave positive reactions only in the case of blood of groups O and A_2, a result which was confirmed by Race and Sanger (1950) and Hubinont (1949). In the second place the results obtained were not quite those which might have been expected. Ikin et al. (1952) in tests on 1166 individuals found the following distribution of phenotypes:

Le(a+b-)	.....	21.10%
Le(a-b+)	.....	71.61%
Le(a-b-)	.....	7.29%

Further it must be added that although the fourth phenotype Le(a+b+) was not found in the British Isles it was found among Australian whites, (Simmons & Jakobowicz 1951) their figures for the distribution of phenotypes being as follows:

Le(a+b-)	26.40%
Le(a-b+)	69.80%
Le(a-b-)	3.60%
Le(a+b+)	0.20%

Writing in 1950 Race and Sanger stated that the results then obtained required at least three alleles to explain them. More recent work, however, has made it clear that the real solution lies in a totally different direction.

Three observations in particular have radically altered the conception of the Lewis system. The first was the discovery of Grubb (1948) that the Lewis system was related to the ABH secretion system when he observed that, without any known exception persons whose cells are Le(a-) are also salivary non-secretors of ABH substances.

The second observation was that of Brendemoen (1949) who found that all persons who were Le(a-) secreted Le^a in their saliva whilst most Le(a-) persons secreted Le^a but the reactions, in the latter case, with anti-Le^a were much weaker than in the former. He also observed that persons who are Le(a+) contain Le^a in their serum whilst persons who are Le(a-) do not.

Finally we must refer to the work of Sneath and Sneath (1955) who found that red cells which lack either Le^a or Le^b will adsorb these antigens if suspended in plasma containing such antigens thus changing the grouping of the cells. It thus appears that the red cell antigens of the Lewis system are not under direct genetic control; they are acquired by the red cells from antigens in the plasma.

The current conception of the Lewis system, as seen in the light of the more recent work, is to quote Grubb: that

> "le systeme de groupe Lewis n'est pas principalement un systeme de groupe sanguin, mais un systeme serologique de mucoides hydrosolubles."

Grubb has proposed a theory under which the presence of the Le^a antigen in the saliva is governed by a gene L which is dominant to its allele (l). He was also able to show that L and l were distinct from the ABH secretor genes, although there is clearly some relationship between the two secretion systems since ABH non-secretors secrete more Le^a than do ABH secretors.

What Race and Sanger (1958) insist is only an aide mémoire nevertheless provides a very convenient way of thinking about the Lewis system. They envisage a limited amount of substrate which can be made into ABH or Le^a substances. The demands of the ABO genes are satisfied first and therefore in ABH secretors there is little substrate available for the L gene to turn into Le^a substance. A little of the latter reaches the saliva but insufficient reaches the plasma for the red cells to adsorb it and give a positive reaction to anti-Le^a. In the case of ABH non-secretors, however, there is sufficient substrate for the L gene to produce enough Le^a substance to enable the red cells to adsorb sufficient Le^a to give a positive reaction with anti-Le^a.

The position of Le^b in this scheme of things is uncertain. Ceppellini regards Le^b as merely a product of Se and L. Race and Sanger (1958) state

that "We try to think of Le^b as little as possible", and we may follow their excellent example, for in the present state of knowledge relating to the Lewis system there is little that can be usefully said here.

It remains to give the various frequencies relating to the gene L as required by Grubb's theory of the Lewis system. There are few published figures available. Those given by Grubb based on tests on 1000 Swedish persons are as follows:

Le^a present in saliva - 90.2%

Le^a absent from saliva - 9.8%

The corresponding gene frequencies are therefore:

L 0.6870

l 0.3130

The genotype frequencies would therefore be:

LL - $(0.6870)^2$ - 0.4721

Ll - $2(0.6870 \times 0.3130)$ - 0.4300

ll - $(0.3130)^2$ - 0.0979

INHERITANCE OF THE LEWIS SYSTEM

Recent work has rendered the earlier inheritance studies obsolete but it is perhaps worth quoting at least one of the earlier analyses to show how even the most convincing evidence can at times be misleading.

Matings			Children				
				Le(a+)		Le(a-)	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
Le(a+) x Le(a+)	18	23.25	39	39	39.00	0.	0.00
Le(a+) x Le(a-)	167	161.19	359	130	115.31	229	243.69
Le(a-) x Le(a-)	279	279.56	627	72	64.71	555	562.29
Total	464		1025	241		784	

The result is an apparently satisfactory fit. Race and Sanger (1950), commenting upon part of the results incorporated in the above tables stated "The agreement is seen to be so close as to leave no doubt that the theory is correct". That in their third edition they state "it now appears that the theory is fundamentally wrong" is a tribute to the extraordinary speed with which serological work is being pushed forward at the moment and a warning against too facile acceptance of apparently satisfactory results.

On the basis of the frequency figures given by Grubb for the L and l genes a provisional inheritance table may be constructed, although there are, as yet, insufficient published figures with which to compare it. On the assumption that Grubb's theory is correct the following represents the expected distribution of mating types and offspring:

Matings		Children		
Type	Frequency	LL	Ll	ll
LL x LL	0.2228	0.2228	—	—
LL x Ll	0.4055	0.20275	0.20275	—
Ll x Ll	0.1849	0.046225	0.09245	0.046225
LL x ll	0.0925	—	0.0925	—
Ll x ll	0.0843	—	0.04215	0.04215
ll x ll	0.0096	—	—	0.0096

THE DEVELOPMENT OF THE LEWIS ANTIGENS

The Lewis system, when considered from the point of view of the development of its antigens, retains its reputation for complexity and uniqueness.

Tests by Race and Sanger (1954) and Jordal (1956) indicate that in foetal blood the phenotype is always Le(a-b-) whilst tests by Rosenfield and Ohno (1953) and Unger (1953) showed the same results from cord blood.

Shortly after birth, however, the antigens appear and tests on children of three months show 80% of them Le(a-); it is not until the age of two years is reached that the adult frequencies are observed. If the Le^a antigen is commoner in young children than in adults, it appears that the antigen Le^b is rarer, and it is not until the age of six years is reached that the adult frequency is observed.

Age is not the only factor which affects the Lewis antigens. The work of Brendemoen (1952) shows that pregnancy is another factor, the agglutinability of cells being considerably reduced during pregnancy. We have been unable to discover how long after the termination of pregnancy it takes for normal agglutinability to be restored - a factor which might be significant if the Lewis system were ever used in disputed paternity proceedings.

"PUBLIC" ANTIGENS

Under this heading are described certain antigens of very high incidence which have not yet been shown to be part of any other system. It is perhaps important to emphasise the somewhat tentative character of this group of antigens, for at least two antigens, previously described as "public" have now been attached to other systems (U to the MNSs system and Tj^a to the P system) and it may well be that a similar fate awaits those that remain in this category.

The Vel antigen: This was first described by Sussman and Miller (1952). The antibody reacted with all but four out of 10,000 samples. Two examples of anti-Vel have now been reported, but there seems to be little information available as to the mode of operation of the antigen.

The Yt^a antigen: Eaton et al. (1956) reported a second antigen of apparently very high incidence. Tests on 1,051 reveal that 88.4% of individuals are homozygous for the antigen, another 11.2% being heterozygous (Yt^a being assumed to act as a dominant). Assuming, therefore, an allele Yt^b the expected gene frequencies are

Yt^a 0.9401

Yt^b 0.0599

BACTERIOGENIC PAN-AGGLUTINATION

A subject to which reference must be made, and which may conveniently be dealt with in connection with "public" antigens, is that concerned with bacteriogenic agglutination - on the basis that the phenomenon is "public" rather than that it is antigenic.

It has been known for some time (Friedenreich, 1930) that either cells or serum may be acted upon by bacteria and viruses in such a way that the cells become agglutinable by all sera, and the serum becomes capable of agglutinating all cells. The phenomenon whereby cells become pan-agglutinable is known as the Hubener-Thomsen-Friedenreich phenomenon and is explained as the result of action by a bacterial enzyme on a latent antigen found on all human cells which turn it into an active antigen. This antigen Friedenreich called T, and it has been found that all normal adult sera contains anti-T, so that all human sera will agglutinate cells which have been subjected to the action of the bacterial enzyme which turns T from a latent to an active antigen.

Pan-agglutinating serum was described by Davidsohn and Tcharsky (1940) when they showed that normal human serum when infected with certain strains of bacteria (which they called H) became capable of agglutinating all samples of human red cells. This was explained on the basis that the bacterial action produced anti-h agglutinins which acted on a H antigen found in all human cells.

"PRIVATE" ANTIGENS

Under this heading are described various antigens of extremely low incidence which have not yet been identified as belonging to any other system. As in the case of the "public" antigens, many of the "private" antigens eventually find their way into one or other of the established systems. Thus the antigens Hu, He, Mi^a and Vw, originally described as "private" antigens have now been shown to be related to the MNSs system, and more recently (Simmons et al. - quoted Race and Sanger 1958) it has been shown that another so-called "private" antigen, known as Graydon, is in fact identical with Vw, and is thus part of the MNSs system.

Those antigens which survive as "private" will be briefly noted. The first of these is the Levay antigen first described by Callender and Race in 1946. Apart from the three persons in the original family no other example appears to have been reported.

The Jobbins antigen was described by Gilbey in 1947, but again no further examples appear to have been reported. The same is also true of the Becker antigen (Elbel and Prokop, 1951) and the Ven antigen (van Loghem and van der Hart, 1952). Several examples, however, have been found of the antigen Wr^a (Holman, 1953). How much longer Wr^a remains relegated to the "private" category has yet to be seen, but if many more examples are found, and it cannot be shown that it is part of any other system it will presumably qualify to graduate as an independent blood group system.

The antigen Be^a (Davidsohn et al. 1953) appears to remain strictly private as do the Ca (Wiener and Brancato 1953), Rm (van der Hart et al. 1954) and By (Simmons and Were, 1955) antigens. More recently, however, yet a further "private" antigen has been reported (Giblett, 1958) which has been christened Js. This appears to be one of the antigens which distinguish negro and white blood, and although rare in white blood has an incidence of about 20% in American negroes.

The same is true of the Di^a (Layrisse et al 1955) which, although "private" so far as Europeans are concerned has been shown to have a moderately high incidence in South American Indians, Chinese and Japanese.

Another rare antigen, which may provisionally be classified as "private" is Chr^a (Kissmeyer-Nielson, 1955) about which little seems to be known at the moment. Yet another antigen, Brugman, was reported by van der Hart (1954) but this appears to have disappeared from the more recent literature, so that it may well have been shown to be identical with some other antigen, but if so we have been unable to trace the reference. Finally, reference should be made to a rather elusive antigen, first recorded by Wiener (1942) but of which nothing seems to have been heard since, and which appears not even to have been dignified with a name of its own.

One of the major difficulties, at least to the neophyte, in wading through serological literature, is the isolated appearance of some antigen

which seems to disappear from the literature soon after, often without trace. The difficulties are of course formidable and are well illustrated by the difficulties arising in attempts to co-ordinate European and Japanese work in this field.

For many years there were reports of a blood group system known as Q described by Furuhata and Imamura, and it was not until 1954 that Henningsen established that Q was in fact identical with P, although this had been suspected for some time. Two other Japanese blood groups I (Iseki and Makino, 1951) and J (Iseki and Makino, 1952) but the antibodies involved have since been established as anti-c and anti-Le^a respectively.

Other factors, references to which are to be found in the earlier literature are:

1) Factor G (Schiff, 1932) the existence of which was demonstrated with immune rabbit serum. It may be added that a second factor, H, reported by Schiff at the same time was later shown by Schiff himself (1934) to be related to the P system, when he identified the anti-body as anti-P.

2) Factor X (Andresen, 1935) whose existence was also demonstrated by the use of immune rabbit sera. It has been suggested that this factor might be related to the P system but if this has been shown we have been unable to trace the reference.

3) Factor E (Sugishita, 1935) the existence of this factor was demonstrated by the use of eel serum. Wiener (1946) has suggested that the properties of E and e are related to or identical with those demonstrable with anti-O sera, or as it should presumably now be called anti-H.

Wiener (1946) refers to various irregular isoagglutinins which have been reported from time to time, and in particular to "extra-agglutinin 1" about which little further seems to have been heard.

GENERAL CONSIDERATIONS

We have now completed our survey of the various blood group systems and before proceeding to consider the purely medico-legal applications of such groups we may pause to look back at the groups we have discussed. Taking all the systems together there are now some 57 antigens which can be positively identified and there are some 20 others that are presumed to exist but for which no antibody has yet been discovered. Even confining the scope of our discussion to the 57 positively identifiable antigens the number of individual blood types that they are capable of defining runs into almost astronomical figures, although of course many of the combinations would be so rare that it is unlikely that they would ever be encountered.

Writing in 1950 Race and Sanger calculated that with the then available antisera 29,952 phenotypes were recognisable and emphasised that this figure represented what could be achieved in practice rather than in theory. This involved the use of 17 antisera. The number of available antisera has been increased since then and the number of phenotypes that can be distinguished in practice has correspondingly risen.

The way in which these blood groups occur in practice can be seen from the results obtained by comprehensive testing. Race and Sanger (1949) using 16 antisera on 250 indivisuals found 178 different blood group combinations of which 132 occurred only once, 28 twice, 11 three times, 6 four times, and 1 five times. A similar analysis by Bertinshaw

et al. (1950) using 17 antisera on 475 individuals revealed 296 different combinations of which 211 occurred only once, the distribution of the others being as follows:

45	occurred	twice
17	"	three times
9	"	four times
7	"	five times
1	"	six times
4	"	seven times
1	"	eight times
1	"	ten times

The commonest English blood group combination is

O, Ms/Ns, P_1, CDe/cde, Lu(a-), Le(a-b+), Fy(a+b+), K-, Jk(a+b+)

and even this occurs only once in every 270 persons.

One final matter which may be mentioned is the suggestion of Professor Sir Ronald Fisher that the usefulness of the various systems may be compared by comparing the sum of the phenotype frequencies. The figure obtained represents the percentage failures of the system to distinguish between two random samples of blood. On this basis we quote the figures given by Race and Sanger (1950) and compare them with those given by the same authors in 1958. The former figures were based on the use of 17 antisera, the latter on the use of 22 antisera which may be taken as those normally available for testing at that date. The figures are as follows:

System	1958	1950
MNSs	16.4	20.0
Rh	19.5	19.5
A_1A_2BO	32.8	32.8
Kidd	37.5	——
Duffy	38.3	53.8
Lewis	56.7	64.8
P	66.6	61.5
Kell	83.7	81.7
Lutheran	85.9	85.4

The major developments over the last eight years can be clearly seen from the above. The Kidd system was not known in 1950 and anti-s had not then been discovered. The use of anti-s has made the MNSs system the most "useful", whilst the use of anti-Fy^b, which was also not identified in 1951 has considerably increased the "usefulness" of the Duffy system.

Such, however, are the blood groups as they stand at the end of 1958, or to speak more accurately, as they are known to the writer at that date, but before turning to consider the medico-legal applications of this knowledge, it will be worth while briefly to mention the more recently discovered "serum groups" the medico-legal applications of which are so similar to those of the more orthodox blood groups.

SERUM GROUPS

In addition to the antigenic blood groups described above a number of serum groups have more recently been discovered. It has thus been found that human sera which is a complex substance contains a type of protein known as serum globulin. Serum globulin can be separated by electrophoretic methods into three fractions; the α , β and γ fractions, whilst the α and β fractions can be still further divided into α_1 , and α_2 , and β_1 , and β_2 fractions. It is differences which have been discovered in the various globulin fractions which have enabled human sera to be divided into groups in a way similar to that in which blood groups antigens divide human blood.

The Haptoglobin Groups: Haptoglobins were first discovered by Jayle (1939) when he reported the existence of haemoglobin binding substances which appeared to be associated with the α_2 globulin fraction. Smithies (1955) using electrophoretic techniques reported the existence of three distinct types of haptoglobins, and in 1955 Smithies and Walker showed that these differences were probably inherited and advanced a theory of inheritance according to which the serum groups were determined by two autosomal genes with incomplete dominance. The three types were originally christened Group I, Group IIA and Group IIB, but a new nomenclature has now been adopted as follows:

Old Nomenclature	New Nomenclature	Genotype
Group I	Haptoglobin 1-1	Hp^1/Hp^1
Group IIA	Haptoglobin 2-1	Hp^2/Hp^1
Group IIB	Haptoglobin 2-2	Hp^2/Hp^2

Galatius-Jensen (1957) studied 1033 unrelated individuals and obtained the following results:

Phenotype	Males		Females		Total	
	obs.	exp.	obs.	exp.	obs.	exp.
Hp 1-1	42	40	133	135	175	168
Hp 2-2	88	86	287	289	375	368
Hp 2-1	108	111	375	372	483	497
Total	238	237	795	796	1033	1033

Using the totals from the above table the gene frequencies can be calculated in the usual way:

$$Hp^1 = 0.169 = \frac{0.468}{2} = 0.403$$

$$Hp^2 = 0.363 = \frac{0.468}{2} = 0.597$$

The phenotype frequencies are therefore

$$\text{Hp 1-1} = (0.403)^2 = 0.1624$$

$$\text{Hp 2-2} = (0.597)^2 = 0.3564$$

$$\text{Hp 1-2} = 2(0.403 \times 0.597) = 0.4812$$

These figures may be compared with the percentage frequencies which can be extracted from the results obtained by Galatius-Jensen, quoted above, which are

Hp 1-1 ..... 16.93%
Hp 2-2 ..... 36.29%
Hp 1-2 ..... 46.76%

This shows reasonable internal consistency in the figures.

Family data studies are also available on the haptoglobins (Galatius-Jensen, 1957) the results of which are summarised in the following table:

Matings			Children					
			Hp 1-1		Hp 2-1		Hp 2-2	
Type	obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.
Hp 1-1 x Hp 1-1	4	2.6	7	7.0	0	0.0	0	0.0
Hp 1-1 x Hp 2-1	15	15.5	20	19.5	19	19.5	0.	0.0
Hp 1-1 x Hp 2-2	13	11.6	0	0.0	29	29.0	0	0.0
Hp 2-2 x Hp 2-1	43	34.1	0	0.0	64	60.0	56	60.0
Hp 2-2 x Hp 2-2	9	12.7	0	0.0	0	0.0	25	25.0
Hp 2-1 x Hp 2-1	22	22.8	10	12.5	26	25.0	14	12.5
Total	106		37		138		95	

These results show reasonably close agreement, with those expected, sufficiently close for the theory of two autosomal genes with incomplete dominance to be regarded as a satisfactory working hypothesis.

It is worth noting that the haptoglobins are not well developed in early childhood, but by the age of four months poorly developed haptoglobins were rare. Even in some adults, it appears, haptoglobins remain rather undeveloped, a condition which may well be hereditary.

Galatius-Jensen regards the haptoglobins as sufficiently well established to justify their use in forensic cases, and speaking of the Danish Institute of Forensic Medicine, he states, "the electrophoretic examination of sera in paternity cases will henceforth be used on an increasing scale."

The Gm Serum Groups: A second and independent system of serum groups was discovered by Grubb (1956) when he found that although some rheumatoid arthritic sera would agglutinate Rh positive cells coated with some incomplete anti-Rh, this agglutination was inhibited in a percentage of normal human sera, so that human sera could be divided into two groups by serological methods. Grubb and Laurell (1956) showed that the inhibitor was located in the gamma-globulin fraction, and in 1957 the same writers showed that the Gm serum groups, as they were called, were probably independent of the haptoglobin groups and also of the ABH and Lewis secretor systems (although it should perhaps be emphasised that this conclusion was based on tests on only 46 persons.)

The two serum groups that were thus established were christened Gm(a+) and Gm(a-), Gm(a+) being the group that inhibits the agglutinating effect of rheumatic arthritic sera on coated Rh positive cells.

The Swedish figures for the frequency distribution of these two phenotypes, based on tests on 360 persons gave the following frequencies:

Gm(a+) 215
Gm(a-) 145

Assuming that the groups are dependent upon the existence of two allelomorphs the corresponding gene frequencies are therefore:

Gm^a 0.3653
Gm 0.6347

Family studies carried out by Grubb and Laurell gave the following results:

Matings			Children				
				Gm(a+)		Gm(a-)	
Type	obs.	exp.	Total	obs.	exp.	obs.	exp.
Gm(a+) x Gm(a+)	9	10	33	30	28.0	3	5.0
Gm(a+) x Gm(a-)	14	13.5	37	25	22.6	12	14.4
Gm(a-) x Gm(a-)	5	4.5	24	0	0.0	24	24.0
Total	28		94	55		39	

These results can be taken, at the very least, as being consistent with a theory of inheritance based on two alleles with Gm^a dominant over Gm.

The published results are scarcely sufficient, as yet, for the medico-legal applications of these groups to be fully realised, yet it is clear that once the theory of inheritance is fully established they will have much the same application as the more orthodox blood groups.

In any medico-legal application of the Gm groups, however, it will be necessary to bear in mind the findings of Bronnestam and Nilsson (1957) who found that in 73 cases out of 74 the Gm group of the infant was the same as that of the mother. They conclude that the Gm groups are not determined at birth and that the Gm substance is transferred to the infant by placental diffusion. Thus the Gm phenotype of the child is not determined at birth by its own genetic constitution.

ABNORMAL HAEMOGLOBINS

One final point which is worth mentioning here is that some haemoglobin abnormalities are inherited and can be used in much the same way as the more traditional blood groups for medico-legal purposes.

Haemoglobin is a conjugated protein in which the haem - a ferroporphyrin - is the prosthetic group: four haems being attached to the protein moiety. Abnormalities resulting from changes in the haem (such as methaemoglobinaemia and sulphaemoglobinaemia) are normally neither permanent or inherited whereas abnormalities in globin synthesis (the haemoglobinopathies) are invariably both permanent and inherited.

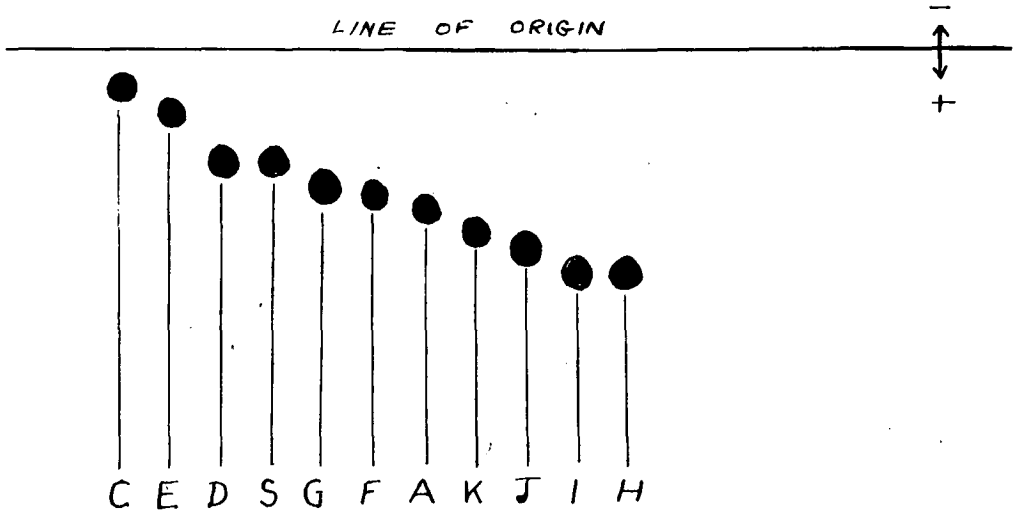
Two normal varieties of haemoglobin are known Adult (A) and Foetal (F). At birth about one half of the child's haemoglobin is foetal, but after four to six months no foetal haemoglobin is normally found and therefore its persistence after six months is usually indicative of some impediment to haemoglobin A production. Thus in a number of haemoglobinopathies the persistence of foetal haemoglobin is found.

The first abnormal haemoglobin to be discovered was haemoglobin S - the haemoglobin associated with thalassaemia and the sickle cell trait. Although the trait was identified by Herrick (1910)it was not until 1949 that Pauling was able to show that sickle cell anaemia was a molecular disease due to abnormal haemoglobin.

Neel (1947) suggested that the distinction between the sickle cell trait anaemia rested on the distinction between the homozygous and heterozygous conditions. This suggestion was subsequently substantiated by Pauling.

The incidence of the sickle cell trait shows the usual geographic variation. The highest frequencies are found in East Africa, with fairly high frequencies in West Africa also. This appears to be related to the fact that the heterozygous condition confers increased immunity to infection of Plasmodium falciparum (malarial infection). The single test that has been reported in relation to Australian aborigines (Horsfall & Lehmann 1953) has failed to reveal the existence of the trait.

In addition to the sickling trait several other varieties of abnormal haemoglobin have been discovered by the application of electrophoretic analysis. In addition to Haemoglobins A, F and S there are now at least eleven known abnormal haemoglobins, which appear to be inherited as Mendelian characteristics: the variants are probably allelomorphs. Eight of these, together with A, F and S are shown on the following diagram which shows their varying electrophoretic mobility:



Electrophoretic mobility of haemoglobin varieties.
Source: Lehmann (1957)

The other three abnormal haemoglobins which appear to be well established are known as L, M and N. In addition to these there are several forms whose identity has not been positively established. These are Buginese X; Galveston type; Hopkins-1 and Hopkins-2.

We may conclude with the observation of Lehmann (1957) that "the haemoglobinoses are also of medico-legal importance." He cites a case, which he observed, in which the sickle cell trait was used as the criterion of exclusion of paternity. Two men were claiming to be the father of a girl. The girl was a sickler but her mother was not. Of the two claimants to paternity only one was a sickler. The other was therefore excluded.

Within a few years it may well be that haemoglobin varieties will have assumed an importance equal to that possessed by the traditional blood groups, but for the immediate present it must be admitted that their use is likely to be very limited.

THE MEDICO-LEGAL APPLICATIONS OF BLOOD GROUP TESTING

The medico-legal applications of blood group testing can be classified under two main heads:

1) the identification of the grouping of blood and secretion stains; and

2) the exclusion of parentage.

Although blood groups will soon celebrate the jubilee of their discovery, and although their medico-legal applications were recognised from the beginning - although whether these were first recognised by von Dungern and Hirszfeld (1910) or by Landsteiner and Richter (1903), as Zinsser and Coca claim, seems not to be settled - their forensic potentialities seem to have been little used in England and Australia compared with the Continent of Europe, and the United States.

The first use of blood group evidence relating to stain identification seems to have occurred in 1916 when Lattes gave evidence in a criminal case before the Italian courts. The first use of blood group evidence for such a purpose did not occur in England until 1929 when Dr. Roche-Lynch gave evidence in a murder trial (R. v. Blakeman). (See also XCIX J.P. & L.G.R 61)

The first use of blood group evidence in disputed paternity proceedings did not occur until 1924 when Schiff gave evidence before a German court whilst the first use, in England, of blood group evidence for such a purpose dates from only 1938. In Wilson v. Wilson Hodson J. (as he then was) accepted such evidence in a nullity suit in which the petitioner sought anulment on the ground that the respondent was, at

the time of the marriage, pregnant by another man. The evidence showed that the child could not have been that of the petitioner, and a decree of nullity was pronounced. (See also Litt v. Litt. (1948))

The English Courts, however, appear to have been preceded in this respect, by both the Irish and the Australian courts. The first application of blood group evidence in a matter pertaining to paternity before the Irish courts seems to have occurred as early as 1932, (Irish L.T. & S.J. 64) whilst a second example was mentioned in the lay press in 1935.

The first mention of the use of such evidence in Australia also dates from 1935 in which year the Australian Law Journal reports an anonymous case in which a maintenance order was quashed after blood group evidence had been considered by the court.

In Hobson v. Hobson (1942) the matter came before the New South Wales courts involving the question of whether the respondent wife was guilty of adultery. The petitioner tendered evidence of blood groups, which had been voluntarily undertaken, showing that he was not the father of a child that had been born to his wife. Bonney J., in accepting the evidence spoke as follows:

"I now come to the real crux of the case - the technical evidence of blood tests tending to show that the petitioner is not the father of the third child. If that is satisfactorily proved, then it would follow that the respondent has committed adultery. This is the first case in this Court in which scientific evidence as to blood tests is solely relied upon, in the last resort, to prove adultery. It is therefore the duty of the Court to examine this method of proof with some care."

The crucial part of his judgment was as follows:

"Am I warranted in accepting this evidence as sufficient proof that the petitioner is not the father of the respondent's child Barry, and that the respondent accordingly committed adultery? On the evidence before me, fortified by a reading of the literature to which the witnesses have referred in their evidence as authoritative, and which they have furnished to me, I see no reason why in this case I should not act upon this evidence. At the present time, and for some years past, longer, of course, in the case of the ABO tests than in the case of the MN tests - these tests have been accepted and acted upon in the Courts of all countries except Italy as evidence of a 'positive negative' character, where they show that a particular man cannot have been the father of the child of a particular woman."

His Honour continued:

"The evidence which has been given in this case, in my judgment, relevant to the issue and I can see no reason to refrain from acting upon it. In this case the standard of proof is, in my view, well above the standard of proof required by the Matrimonial Causes Act, as explained in Briginshaw v. Briginshaw. I am satisfied that the margin of possible error is distinctly less than it is in many cases that are decided in the ordinary way on a conflict of oral evidence."

His Honour held that the respondent was guilty of adultery but declined to hold that she committed adultery with the co-respondent - the blood tests merely showed that he was a possible father and the other evidence was inconclusive.

According to Wiener blood group tests were little used in the United States before 1934. In that year, however, in Beuschel v. Manowitz, the court ordered tests to be taken. The decision in this case was reversed on the ground of lack of statutory authority to order such tests, but shortly thereafter many States introduced legislation authorising the courts to order such tests. (See Appendices II and III)

Blood tests had, however, been used on a voluntary basis rather earlier. This blood group evidence was submitted in Commonwealth v. Zammonelli (1931) in which a new trial was ordered in a bastardy case on the ground that the finding was reached contrary to uncontroverted expert testimony as to the blood groups of the parties.

A Bill authorising such tests was introduced in to the House of Lords in 1938./ (See appendix I) It was favourably received and the Select Committee appointed to consider the Bill reported in favour, but unfortunately, owing to the war, the Bill was not proceeded with. In 1939 a section (s.120) authorising such tests was inserted in the New South Wales Child Welfare Act but the section has not yet been brought into operation./ (See appendix IV).

With this brief introduction we may turn to consider the basis of the medico-legal applications of blood group testing.

MEDICO-LEGAL APPLICATION OF BLOOD GROUPS IN DISPUTED PATERNITY

PROCEEDINGS

The application of blood group testing to disputed paternity proceedings depends on the fundamental principle that no child can possess any gene which is not carried by either of its parents. Thus to consider the case of an ABO mating; if both parents are of group O the child cannot possess an A or B gene for the simple reason that the child's genes are derived exclusively from its parents and if the parents do not carry the gene then neither can the child. In respect of each blood group, therefore, it is possible to construct a table setting out, in relation to each possible mating type, the blood groups which any offspring may possess and the blood groups which their offspring could not possess.

This information has been set out implicitly if not explicitly in the preceding discussion of the various blood group systems, but for the purpose of convenience the various exclusionary tables are collected together here, all of them being constructed on a uniform plan which is adapted from that first used by Boyd in connection with the Rh blood groups. In addition the same information is given in a slightly different form in which is included the frequency of the various mating types. This latter is useful in assessing the efficiency of the system as an exclusionary criterion.

It must be emphasised that much depends upon the availability of the necessary antisera, and where necessary, therefore, exclusionary tables have been constructed separately for the various levels of testing.

ABO SYSTEM

Taking the ABO system in its classical form as comprising the four blood groups, A, B, AB and O, there are ten phenotypically distinct matings to be considered. In the following table the blood groups of the child are set out horizontally and those of the mother vertically. Each of the blood groups is numbered, the numbering being the same for both child and mother. The numbers within each square represent the blood groups which, if possessed by the alleged father would exclude him from paternity. The table has been constructed in this way rather than in the more conventional manner on the ground that since exclusion of paternity is the information that is required it is preferable to have it set out directly and not indirectly.

Blood group of mother	Blood group of child			
	1. A	2. B	3. AB	4. O
1. A	None	1, 4	1, 4	3
2. B	2, 4	None	2, 4	3
3. AB	None	None	4	All
4. O	2, 4	1, 4	All	3

Essentially the same information, set out in relation to each mating type with the frequency of the latter is tabulated below:

Matings		Children	
Type	Frequency	Possible	Impossible
A x A	0.1580	A and O	B and AB
A x B_B	0.0773	All groups	None
A x AB	0.0236	A, B & AB	O
A x O^r	0.3780	A and O	B and AB
B x B	0.0095	B and O	A and AB
B x AB	0.0058	A, B & AB	O
B x O	0.0925	B and O	A and AB
AB x AB	0.0009	A, B & AB	O
AB x O	0.0283	A and B	AB and O
O x O	0.2261	O	A, B and AB

It will be observed that the O x O mating, from which only one type of offspring is possible, constitutes nearly one quarter of all ABO matings, whilst from the A x O mating which comprises over a third of all ABO matings only two types of offspring are possible. On the other hand the A x B mating from which no exclusion is possible may be expected to occur no more frequently than a little over 7% of ABO matings. This factor of the relative frequency of the respective matings must be borne in mind when considering the efficiency of the system as an exclusionary criterion in cases of disputed paternity.

Since there is no certain method of distinguishing between the homozygote and the heterozygote there is little purpose in setting out a full analysis of the genotypically distinct matings. When and if a genuine anti-O serum is discovered then 21 distinct mating types will have to be considered, of which five would only be capable of producing one genotype in their offspring. Thus much finer discrimination would be possible. If Race and Sanger (1958) are to be believed, however, the day when such a degree of discrimination will be possible is still far away.

Leaving aside, therefore, the possibility of testing at that level, the next level at which testing within the ABO system can be undertaken is that which includes the subgroups based upon A_1 and A_2. At this level of testing there are six distinct phenotypes and therefore 21 distinct mating types. Casting the information into the same form as that used for the simple ABO system we obtain the following results:

Blood group of mother	Blood group of child					
	1. A_1	2. A_2	3. B	4. A_1B	5. A_2B	6. O
1. A_1	None	4	1,2,6	1,2,6	1,2,6	4,5
2. A_2	2,3,5,6	4	1,2,6	All	1,2,6	4,5
3. B	2,5,6	3,6	None	2,3,5,6	3,4,6	4,5
4. A_1B	None	All	None	2,6	3,4,6	All
5. A_2B	2,3,5,6	4	None	2,3,5,6	1,6	All
6. O	2,3,5,6	3,4,6	1,2,6	All	All	4,5

It should be noted that those cases in which "All" fathers are excluded are, of course, cases in which maternity is excluded, i.e. a mother of that group could not produce a child of the indicated group whatever blood group had been possessed by the father.

Below the same information is tabulated in relation to each mating, the frequencies of the latter being calculated from the Australian figures for the distribution of the phenotypes which was given earlier:

Matings		Children	
Type	Frequency	Possible	Impossible
$A_1 \times A_1$	0.1216	A_1, A_2 and O	B, A_1B and A_2B
$A_1 \times A_2$	0.0675	A_1, A_2 and O	B, A_1B and A_2B
$A_1 \times B$	0.0589	All groups	None
$A_1 \times A_1B$	0.0178	A_1, B, A_1B and A_2B	A_2 and O
$A_1 \times A_2B$	0.0053	A_1, A_2, B, A_1B, and A_2B	O
$A_1 \times O$	0.3040	A_1, A_2 and O	B, A_1B and A_2B
$A_2 \times A_2$	0.0094	A_2 and O	A_1, B, A_1B and A_2B
$A_2 \times B$	0.0164	A_2, B, O and A_2B	A_1 and A_1B
$A_2 \times A_1B$	0.0049	A_1, B and A_2B	A_2, A_1B and O
$A_2 \times A_2B$	0.0016	A_2, B and A_2B	A_1, A_1B and O
$A_2 \times O$	0.0844	A_2 and O	A_1, B, A_1B and A_2B
$B \times B$	0.0071	B and O	A_2, A_2, A_1B and A_2B
$B \times A_1B$	0.0043	A_1, B and A_1B	A_2, A_2B and O
$B \times A_2B$	0.0014	A_2, B and A_2B	A_1, A_1B and O
$B \times O$	0.0737	B and O	A_1, A_2, A_1B and A_2B
$A_1B \times A_1B$	0.0006	A_1, B and A_1B	A_2, A_2B and O
$A_1B \times A_2B$	0.0004	A_1, B, A_1B and A_2B	A_2 and O
$A_1B \times O$	0.0223	A_1 and B	A_2, A_1B, A_2B and O
$A_2B \times A_2B$	0.0001	A_2, B and A_2B	A_1, A_1B and O
$A_2B \times O$	0.0074	A_2 and B	A_1, A_1B, A_2B and O
$O \times O$	0.2392	O	A_1, A_2, B, A_1B and A_2B

Just as there was no justification for dealing with genotypic differences in the main ABO system, so there is no justification for dealing with them in connection with the sub-groups. It will be realised, of course, that if it ever becomes possible to distinguish between the homozygote and the heterozygote the degree of discrimination achieved by the ABO system, including the sub-groups A_1 and A_2 will be vastly increased. There would then be ten recognisable phenotypes and therefore 55 distinct mating types, but before such testing becomes possible a reliable and genuine anti-O serum must be found.

There is also little point in compiling exclusion tables taking into account such rarities as A_3, B_x or B_3. They add considerably to the complexity of exclusion without really adding much to their usefulness. If, and when, examples are encountered the problems can easily be worked out from first principles.

MN SYSTEM

We may consider first the original MN system with its three distinguishable phenotypes, M, N and MN and its six phenotypically distinct matings. Casting the information in the form adopted for the ABO system we obtain the following results:

Blood group of mother	Blood group of child		
	1. M	2. MN	3. N
1. M	3	1	All
2. MN	3	None	1
3. N	All	3	1

The same information when cast into the alternative form appears as follows:

Matings		Phenotype of Children	
Type	Frequency	Possible	Impossible
M x M	0.0799	M	MN and N
M x MN	0.2815	M and MN	N
M x N	0.1240	MN	M and N
MN x MN	0.2479	M, MN and N	None
MN x N	0.2184	MN and N	M
N x N	0.0481	N	M and MN

When the system as extended by S and s is considered then the picture becomes very much more complex. Ten distinct phenotypes can be recognised and 55 phenotypically distinct mating types. The relevant information is tabulated in the attached tables which follow the same pattern as those used earlier.

The first two tables set out the position where anti-S alone is used, whilst the third table sets out that which is achieved by the use of both anti-S and anti-s. The frequency of the various mating types distinguishable by the use of anti-s has already been set out, and in view of the complexity of the table it was thought unnecessary to set out the information again here.

Blood group of mother	Blood group of child					
	1. Ms/Ms	2. MM.S	3. Ms/Ns	4. MN.S	5. Ns/Ns	6. NN.S
1. Ms/Ms	5,6	1,5,6	1,2	1,2,5	All	All
2. MM.S	5,6	5,6	1,2	1,2	All	All
3. Ms/Ns	5,6	5,6	None	1,5	1,2	1,2,5
4. MN.S	5,6	5,6	None	None	1,2	5,6
5. Ns/Ns	All	All	5,6	1,3,5,6	1,2	1,2,5
6. NN.S	All	All	5,6	5,6	1,2	1,2

Matings		Children	
Type	Frequency	Possible	Impossible
Ms/Ms x Ms/Ms	0.0064	Ms/Ms	MM.S, Ms/Ns, MN.S, Ns/Ns & NN.S
Ms/Ms x MM.S	0.0032	Ms/Ms and MM.S	Ms/Ns, MN.S, Ns/Ns & NN.S
MM.S x MM.S	0.0404	Ms/Ms and MM.S	Ms/Ns, MN.S, Ns/Ns & NN.S
Ms/Ms x Ms/Ns	0.0345	Ms/Ms and Ms/Ns	MM.S, MN.S, Ns/Ns & NN.S
MM.S x Ms/Ns	0.0887	Ms/Ms, MM.S, Ms/Ns and MN.S	Ns/Ns and NN.S
Ms/Ms x MN.S	0.0445	Ms/Ms, MM.S, Ms/Ns and MN.S	Ns/Ns and NN.S
MM.S x MN.S	0.1116	Ms/Ms, MM.S, Ms/Ns and MN.S	Ns/Ns and NN.S
Ms/Ms x Ns/Ns	0.0243	Ms/Ns	Ms/Ms, MM.S., MN.S, Ns/Ns & NN.S
MM.S x Ns/Ns	0.0610	Ms/Ns and MN.S	Ms/Ms, MM.S., Ns/Ns & NN.S
Ms/Ms x NN.S	0.0111	Ms/Ns and MN.S	Ms/Ms, MM.S, Ns/Ns & NN.S
MM.S x NN.S	0.0277	Ms/Ns and MN.S	Ms/Ms, MM.S, Ns/Ns & NN.S
Ms/Ns x Ms/Ns	0.0486	Ms/Ms, Ms/Ns and Ns/Ns	MM.S, MN.S & NN.S
MN.S x Ms/Ns	0.1225	Ms/Ms, MM.S, Ms.Ns, MN.S, Ns/Ns, NN.S.	NONE
MN.S x MN.S	0.0771	Ms/Ms, MM.S, Ms/Ns, MN.S, Ns/Ns, &NN.S.	NONE
Ms/Ns x Ns/Ns	0.0669	Ms/Ns and Ns/Ns	Ms/Ms, MM.S, MN.S & NN.S
MN.S x Ns/Ns	0.0842	Ms/Ns, MN.S, Ns/Ns and NN.S	Ms/Ms and MM.S
MN.S x NN.S	0.0383	Ms/Ns, MN.S, Ns/Ns and NN.S	Ms/Ms and MM.S
Ms/Ns x NN.S	0.0304	Ms/Ns, MN.S, Ns/Ns and NN.S	Ms/Ms and MM.S
Ns/Ns x Ns/Ns	0.0230	Ns/Ns	Ms/Ms, MM.S, Ms/Ns, MN.S & NN.S
NN.S x NN.S	0.0048	Ns/Ns and NN.S	Ms/Ms, MM.S, Ms/Ns and MN.S
NN.S x Ns/Ns	0.0209	Ns/Ns and NN.S	Ms/Ms, MM.S, Ms/Ns and MN.S

Blood group of mother	Blood group of child									
	1. MS/MS	2. MS/Ms	3. Ms/Ms	4. MS/NS	5. MS/Ns	6. Ms/NS	7. Ms/Ns	8. NS/NS	9. NS/Ns	10. Ns/Ns
1. MS/MS	3,6,7,8,9,10	1,4,5,8,9,10	All	1,2,3,5,7,10	1,2,3,4,6,8	All	All	All	All	All
2. MS/Ms	3,6,7,8,9,10	8,9,10	1,4,5,8,9,10	1,2,3,5,7,10	1,2,3,4,6,8	1,2,3,5,7,10	1,2,3,4,6,8	All	All	All
3. Ms/Ms	All	3,6,7,8,9,10	1,4,5,8,9,10	All	All	1,2,3,5,7,10	1,2,3,4,6,8	All	All	All
4. MS/NS	3,6,7,8,9,10	1,4,5,8,9,10	All	3,7,10	1,2,3,4,6,8	1,4,5,8,9,10	All	1,2,3,5,7,10	1,2,3,4,6,8	All
5. MS/Ns	3,6,7,8,9,10	1,4,5,8,9,10	All	1,2,3,5,7,10	3,6,8	All	1,4,5,8,9,10	All	1,2,3,5,7,10	1,2,3,4,6,8
6. Ms/NS	All	3,6,7,8,9,10	1,4,5,8,9,10	3,6,7,8,9,10	3,6,8	1,5,10	1,2,3,4,6,8	1,2,3,5,7,10	1,2,3,4,6,8	All
7. Ms/Ns	All	3,6,7,8,9,10	1,4,5,8,9,10	All	3,6,7,8,9,10	1,2,3,5,7,10	1,4,8	All	1,2,3,5,7,10	1,2,3,4,6,8
8. NS/NS	All	All	All	3,6,7,8,9,10	All	1,4,5,8,9,10	All	1,2,3,5,7,10	1,2,3,4,6,8	All
9. NS/Ns	All	All	All	3,6,7,8,9,10	3,6,7,8,9,10	1,4,5,8,9,10	1,4,5,8,9,10	1,2,3,5,7,10	1,2,3,	1,2,3,4,6,8
10. Ns/Ns	All	All	All	All	3,6,7,8,9,10	All	1,4,5,8,9,10	All	1,2,3,5,7,10	1,2,3,4,6,8

The numbers within the squares represent the genotypes which, if possessed by the alleged father, would exclude him from paternity.

Whilst, of course, the rare antigens cannot be ignored in problems of paternity, it is hardly necessary to take them into account in the construction of the basic exclusion tables. Thus neither the rare alleles of M, N, or S such as M_2, N_2, M^c, M^g and S^u, or such "private" antigens as Hu, He, Mi^a and Vw have been considered in the foregoing account. That being so there are no further levels of testing within the MNSs system that need be considered here.

THE P BLOOD GROUP SYSTEM

If we consider the P system as extended by Sanger (1955) to include the earlier Jay system then there are three distinguishable phenotypes and therefore six phenotypically distinct mating types. The extreme rarity of (p) - or, as it was known earlier Tj^b - makes it unnecessary to set out exclusionary tables which include this antigen. If this be disregarded then the situation is almost exactly that to be found in the unextended P system. For convenience, therefore, the exclusionary data derived from the P system is tabulated using the nomenclature of the unextended system.

Blood group of mother	Blood group of child	
	1. P+	2. P-
1. P+	None	None
2. P-	2	None

Mating		Children	
Type	Frequency	Poss.	Imposs.
P+ x P+	0.6217	Both	None
P+ x P-	0.3336	Both	None
P- x P-	0.0447	P-	P+

Since P- x P- matings represent only about 5% of all matings and since this is the only mating in which an exclusion is possible, the efficiency of the P system can be seen to be rather low.

THE Rh BLOOD GROUP SYSTEM

The Rh system must obviously be considered at various levels of testing. The primary level of testing, involving the use of only anti-D is hardly worth considering in this context. An exclusion is only possible in the case of an Rh- x Rh- mating, and these only constitute 2.5% of all matings, so that from the point of view of exclusion of possible paternity such testing is of little significance.

The first level of testing which is worth considering in this context is that involving the use of the three antisera anti-C, anti-D and anti-E. At this level eight phenotypes are distinguishable with, therefore, 36 mating types to be considered. The exclusionary potentialities of the Rh system, at this level, can be seen from the two following tables which are constructed on the same basis as those used earlier in relation to the other groups.

It will be noted that, taking into account the expected frequencies of the various mating types, no exclusion in a little under half (44.8%) of all matings, so that, at this level, the Rh system cannot be ranked as very efficient, although of course with the use of additional antisera the efficiency of the system is increased.

Blood group of mother	Blood group of child							
	1. CDE	2. CDee	3. CddE	4. Cddee	5. ccDE	6. ccDee	7. ccddE	8. ccddee
1. CDE	None	None	None	None	None	None	None	None
2. CDee	2, 4, 6, 8	None	2, 4, 6, 8	None	2, 4, 6, 8	None	2, 4, 6, 8	None
3. CddE	3, 4, 7, 8	3, 4, 7, 8	None	None	3, 4, 7, 8	3, 4, 7, 8	None	None
4. Cddee	2, 3, 4, 6, 7, 8	3, 4, 7, 8	2, 4, 6, 8	None	2, 3, 4, 6, 7, 8	3, 4, 7, 8	2, 4, 6, 8	None
5. ccDE	5, 6, 7, 8	5, 6, 7, 8	5, 6, 7, 8	5, 6, 7, 8	None	None	None	None
6. ccDee	2, 4, 5, 6, 7, 8	5, 6, 7, 8	2, 4, 5, 6, 7, 8	5, 6, 7, 8	2, 4, 6, 8	None	2, 4, 6, 8	None
7. ccddE	3, 4, 5, 6, 7, 8	3, 4, 5, 6, 7, 8	5, 6, 7, 8	5, 6, 7, 8	3, 4, 7, 8	3, 4, 7, 8	None	None
8. ccddee	2, 3, 4, 5, 6, 7, 8	3, 4, 5, 6, 7, 8	2, 4, 5, 6, 7, 8	5, 6, 7 8	2, 3, 4, 6, 7, 8	3, 4, 7, 8	2, 4, 6, 8	None

Matings		Children	
Type	Frequency	Possible	Impossible
CDE x CDE	0.02746	All	None
CDE x ccDE	0.04166	All	None
CDE x CddE	0.00000	All	None
CDE x CDee	0.1789	All	None
CDE x ccddE	0.00189	All	None
CDE x ccDee	0.00189	All	None
CDE x Cddee	0.00285	All	None
CDE x ccddee	0.04923	All	None
ccDE x ccDE	0.01581	ccDE, ccddE, ccDee & ccddee	CDE, CddE, CDee & Cddee
ccDE x CddE	0.00000	All	None
ccDE x CDee	0.1358	All	None
ccDE x ccddE	0.00143	ccDE, ccddE, ccDee & ccddee	CDE, CddE, CDee & Cddee
ccDE x ccDee	0.00143	ccDE, ccddE, ccDee & ccddee	CDE, CddE, CDee & Cddee
ccDE x Cddee	0.00216	All	None
ccDE x ccddee	0.03736	ccDE, ccddE, ccDee & ccddee	CDE, CddE, CDee & Cdee
CddE x CddE	0.00000	CddE, ccddE, Cddee & ccddee	CDE, CDee, ccDE & ccDee
CddE x CDee	0.00000	All	None
CddE x ccddE	0.00000	CddE, ccddE, Cddee & ccddee	CDE, CDee, ccDE & ccDee
CddE x ccDee	0.00000	All	None
CddE x Cddee	0.00000	CddE, ccddE, Cddee & ccddee	CDE, CDee, ccDE & ccDee
CddE x ccddee	0.00000	CddE, ccddE, Cddee & ccddee	CDE, CDee, ccDE & ccDee
CDee x CDee	0.2196	CDee, ccDee, Cddee & ccddee	CDE, CddE, ccDE & ccddE
CDee x ccddE	0.00616	All	None
CDee x ccDee	0.00616	CDee, ccDee, Cddee & ccddee	CDE, CddE, ccDE & ccddE
CDee x Cddee	0.00929	CDee, ccDee, Cddee & ccddee	CDE, CddE, ccDE & ccddE
CDee x ccddee	0.1640	CDee, ccDee, Cddee & ccddee	CDE, CddE, ccDE & ccddE
ccddE x ccddE	0.00003	ccddE and ccddee	CDE, CddE, CDee, ccDE, ccDee & Cddee
ccddE x ccDee	0.00006	ccDee, ccDE, ccddE & ccddee	CDE, CddE, CDee & Cddee
ccddE x Cddee	0.00010	CddE, ccddE, Cddee & ccddee	CDE, CDee, ccDE & ccDee
ccddE x ccddee	0.00173	ccddE & ccddee	CDE, CddE, CDee, ccDE, ccDee & Cddee
ccDee x ccDee	0.00003	ccDee & ccddee	CDE, CddE, CDee, ccDE, ccddE & Cddee
ccDee x Cddee	0.00010	CDee, ccDee, Cddee & ccddee	CDE, CddE, ccDE & ccddE
ccDee x ccddee	0.00173	ccDee & ccddee	CDE, CddE, CDee, ccDE, ccddE & Cddee
Cddee x Cddee	0.00007	Cddee & ccddee	CDE, CddE, CDee, ccDE, ccddE & ccDee
Cddee x ccddee	0.00256	Cddee & ccddee	CDE, CddE, CDee, ccDE, ccddE & ccDee
ccddee x ccddee	0.02208	ccddee	CDE, CddE, CDee, ccDE, ccddE, ccDee & Cddee

The construction of the necessary tables relating to the additional levels of testing in the Rh system presents a problem for a typist, and we have therefore confined ourselves to a single exclusion table showing the position where four antisera are used; anti-C, anti-D, anti-E and anti-c.

Blood group of child

Blood group of mother	1 CCDE	2 CCDee	3 CCddE	4 CCddee	5 CcDE	6 CcDee	7 CcddE	8 Ccddee	9 ccDE	10 ccDee	11 ccddE	12 ccddee
1. CCDE	9,10,11,12	9,10,11,12	9,10,11,12	9,10,11,12	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4	All	All	All	All
2. CCDee	2,4,6,8,9,10,11,12	9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	1,2,3,4,6,8,10,12	1,2,3,4	1,2,3,4,6,8,10,12	1,2,3,4	All	All	All	All
3. CCddE	3,4,7,8,9,10,11,12	3,4,7,8,9,10,11,12	9,10,11,12	9,10,11,12	1,2,3,4,7,8,11,12	1,2,3,4,7,8,11,12	1,2,3,4	1,2,3,4	All	All	All	All
4. CCddee	2,3,4,6,7,8,9,10,11,12	3,4,7,8,9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	1,2,3,4,6,7,8,10,11,12	1,2,3,4,7,8,11,12	1,2,3,4,6,8,10,12	1,2,3,4	All	All	All	All
5. CcDE	9,10,11,12	9,10,11,12	9,10,11,12	9,10,11,12	None	None	None	None	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4
6. CcDee	2,4,6,8,9,10,11,12	9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	2,4,6,8,10,12	None	2,4,6,8,10,12	None	1,2,3,4,6,8,10,12	1,2,3,4	1,2,3,4,6,8,10,12	1,2,3,4
7. CcddE	3,4,7,8,9,10,11,12	3,4,7,8,9,10,11,12	9,10,11,12	9,10,11,12	3,4,7,8,11,12	3,4,7,8,11,12	None	None	1,2,3,4,7,8,11,12	1,2,3,4,7,8,11,12	1,2,3,4	1,2,3,4
8. Ccddee	2,3,4,6,7,8,9,10,11,12	3,4,7,8,9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	2,3,4,6,7,8,10,11,12	3,4,7,8,11,12	2,4,6,8,10,12	None	1,2,3,4,6,7,8,10,11,12	1,2,3,4,7,8,11,12	1,2,3,4,6,8,10,12	1,2,3,4
9. ccDE	All	All	All	All	9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	9,10,11,12	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4
10. ccDee	All	All	All	All	2,4,6,8,9,10,11,12	9,10,11,12	3,4,7,8,9,10,11,12	9,10,11,12	1,2,3,4,6,8,10,12	1,2,3,4	1,2,3,4,6,8,10,12	1,2,3,4
11. ccddE	All	All	All	All	3,4,7,8,9,10,11,12	3,4,7,8,9,10,11,12	9,10,11,12	9,10,11,12	1,2,3,4,7,8,11,12	1,2,3,4,7,8,11,12	1,2,3,4	1,2,3,4
12. ccddee	All	All	All	All	2,6,3,6,7,8,9,10,11,12	3,4,7,8,9,10,11,12	2,4,6,8,9,10,11,12	9,10,11,12	1,2,3,4,6,7,8,10,11,12	1,2,3,4,7,8,11,12	1,2,3,4,6,8,10,12	1,2,3,4

THE LUTHERAN BLOOD GROUP SYSTEM

The Lutheran system need be considered at two levels only. The first involving testing with anti-Lu^a alone, and the second with both anti-Lu^a and anti-Lu^b. The relevant information, at both levels, is tabulated, in the usual form, below.

Blood group of mother	Blood group of child	
	1. Lu(a+)	2. Lu(a-)
1. Lu(a+)	None	None
2. Lu(a-)	2	None

Matings		Children	
Type	Frequency	Possible	Impossible
Lu(a+) x Lu(a+)	0.0058	Both	Neither
Lu(a+) x Lu(a-)	0.1413	Both	Neither
Lu(a-) x Lu(a-)	0.8529	Lu(a-)	Lu(a+)

It will be observed that although an exclusion is only possible in one type of mating, nevertheless that type of mating constitutes 85% of all matings, so that the efficiency of the Lutheran system as an exclusionary criterion is higher than might appear at first sight. Using both antisera the position is as follows:

Blood group of mother	Blood group of child		
	1. Lu^aLu^a	2. Lu^aLu^b	3. Lu^bLu^b
1. Lu^aLu^a	3	1	All
2. Lu^aLu^b	32	None	1
3. Lu^bLu^b	All	3	1

Matings		Children	
Type	Frequency	Possible	Impossible
$Lu^aLu^a \times Lu^aLu^a$	0.0000	Lu^aLu^a	Lu^aLu^b, Lu^bLu^b
$Lu^aLu^a \times Lu^aLu^b$	0.0002	Lu^aLu^a, Lu^aLu^b	Lu^bLu^b
$Lu^aLu^b \times Lu^aLu^b$	0.0056	All	None
$Lu^aLu^a \times Lu^bLu^b$	0.0028	Lu^aLu^b	Lu^aLu^a, Lu^bLu^b
$Lu^aLu^b \times Lu^bLu^b$	0.1385	Lu^aLu^b, Lu^bLu^b	Lu^aLu^a
$Lu^bLu^b \times Lu^bLu^b$	0.8529	Lu^bLu^b	Lu^aLu^a, Lu^aLu^b

THE KELL BLOOD GROUP SYSTEM

Since the position of the more recently discovered Kp^a and Kp^b is s till very uncertain, the Kell system, when considered as an exclusionary criterion in paternity cases, needs to be treated at two levels only; that using anti-K only, and that using both anti-K and anti-k. It will be noted that the situation, at both levels, is very similar to that found in the Lutheran system.

Blood group of mother	Blood group of child	
	1. K+	2. K-
1. K+	None	None
2. K-	2	None

Matings		Children	
Type	Frequency	Possible	Impossible
K+ x K+	0.0080	Both	Neither
K+ x K-	0.1626	Both	Neither
K- x K-	0.8294	K-	K+

As in the case of the Lutheran system the only mating in which there can be an exclusion comprises nearly 83% of all matings thus raising the exclusionary efficiency of the system. If both antisera are used then the position is as follows:

Blood group of mother	Blood group of child		
	1. KK	2. Kk	3. kk
1. KK	3	1	All
2. Kk	3	None	1
3. kk	All	3	1

Matings		Children	
Type	Frequency	Possible	Impossible
KK x KK	0.0000	KK	Kk and kk
KK x Kk	0.0004	KK and Kk	kk
Kk x Kk	0.0076	KK, Kk and kk	None
KK x kk	0.0038	Kk	KK and kk
Kk x kk	0.1588	Kk and kk	KK
kk x kk	0.8294	kk	KK and Kk

THE DUFFY BLOOD GROUP SYSTEM

The Duffy system, when considered as an exclusionary criterion in paternity cases, must be treated in two distinct ways: the first concerns the application of the system to white populations, the second, its application to negroes.

Considering first the application of the system to white populations there are two levels of testing to be taken into account. The first is that which involves the use of anti-Fy^a alone, the second that which involves the use of both anti-Fy^a and anti-Fy^b. The situation where anti-Fy^a alone is used is as follows:

Blood group of mother	Blood group of child	
	1. Fy(a+)	2. Fy(a-)
1. Fy(a+)	None	None
2. Fy(a-)	2	None

Matings		Children	
Type	Frequency	Possible	Impossible
Fy(a+) x Fy(a+)	0.4317	Both	Neither
Fy(a+) x Fy(a-)	0.4507	Both	Neither
Fy(a-) x Fy(a-)	0.1176	Fy(a-)	Fy(a+)

It will be noted that in this case the only mating from which an exclusion is possible comprises only 11% of all matings, so that at this level of testing the exclusionary efficiency of the system is not very great. The situation is, however, improved slightly by the additional use of anti-Fy^b in which case the position is as follows:

Blood group of mother	Blood group of child		
	1. Fy^aFy^a	2. Fy^aFy^b	3. Fy^bFy^b
1. Fy^aFy^a	3	1	All
2. Fy^aFy^b	3	None	1
3. Fy^bFy^b	All	3	1

Matings		Children	
Type	Frequency	Possible	Impossible
$Fy^aFy^a \times Fy^aFy^a$	0.0295	Fy^aFy^a	Fy^aFy^b, Fy^bFy^b
$Fy^aFy^a \times Fy^aFy^b$	0.1667	Fy^aFy^a, Fy^aFy^b	Fy^bFy^b
$Fy^aFy^b \times Fy^aFy^b$	0.2355	All	None
$Fy^aFy^a \times Fy^bFy^b$	0.1178	Fy^aFy^b	Fy^aFy^a, Fy^bFy^b
$Fy^aFy^b \times Fy^bFy^b$	0.3329	Fy^aFy^b, Fy^bFy^b	Fy^aFy^a
$Fy^bFy^b \times Fy^bFy^b$	0.1176	Fy^bFy^b	Fy^aFy^a, Fy^aFy^b

In considering the application of the Duffy system to negroes account must be taken of the phenotype Fy(a-b-). Exclusionary tables may be constructed on the assumption that the occurrence of this phenotype rests on the existence of a third allele Fy. Assuming that this is so then the position would be as follows:

Blood group of mother	Blood group of child			
	1. Fy(a+b-)	2. Fy(a+b+)	3. Fy(a-b+)	4. Fy(a-b-)
1. Fy(a-b-)	1,4	1,2,3	1,2,3,4	1,4
2. Fy(a-b-)	1,2,3	1,2,3,	1,2,3	1,3
3. Fy(a-b-)	1,2,3,4	1,2,3	1,3,4	3,4
4. Fy(a-b-)	1,4	1,3	3,4	4

THE KIDD BLOOD GROUP SYSTEM

Here again it is only necessary to consider the system at two levels. The first being that involving testing with anti-Jk^a the second with both anti-Jk^a and anti-Jk^b. The results are tabulated in the usual form below.

Blood group of mother	Blood group of child	
	1. Jk(a+)	2. Jk(a-)
1. Jk(a+)	None	None
2. Jk(a-)	2	None

Matings		Children	
Type	Frequency	Possible	Impossible
Jk(a+) x Jk(a+)	0.5837	Both	Neither
Jk(a+) x Jk(a-)	0.3606	Both	Neither
Jk(a-) x Jk(a-)	0.0557	Jk(a-)	Jk(a+)

It will be noted that the efficiency of the system as an exclusionary criterion, at this level of testing, is very low, as an exclusion is only possible in the case of Jk(a-) x Jk(a-) matings, and these comprise only about 5% of all marriages. The situation is improved by the use of anti-Jk^b, where the position is as follows:

Blood group of mother	Blood group of child		
	1. Jk^aJk^a	2. Jk^aJk^b	3. Jk^bJk^b
1. Jk^aJk^a	3	1	All
2. Jk^aJk^b	3	None	1
3. Jk^bJk^b	All	3	1

Matings		Children	
Type	Frequency	Possible	Impossible
$Jk^aJk^a \times Jk^aJk^a$	0.0699	Jk^aJk^a	Jk^aJk^b, Jk^bJk^b
$Jk^aJk^a \times Jk^aJk^b$	0.2642	Jk^aJk^a, Jk^aJk^b	Jk^bJk^b
$Jk^aJk^b \times Jk^aJk^b$	0.2496	All	None
$Jk^aJk^a \times Jk^bJk^b$	0.1248	Jk^aJk^b	Jk^aJk^a, Jk^bJk^b
$Jk^aJk^b \times Jk^bJk^b$	0.2358	Jk^aJk^b, Jk^bJk^b	Jk^aJk^a
$Jk^bJk^b \times Jk^bJk^b$	0.0557	Jk^bJk^b	Jk^aJk^a, Jk^aJk^b

THE ABH SECRETION SYSTEM

The secretor system, although not a blood group system, properly so-called, may nevertheless be employed as an exclusionary criterion in paternity cases on exactly the same basis as the blood groups themselves. The relevant information is tabulated below in the usual form, using Se to denote the dominant gene and se the recessive.

Mother	Child	
	1. Se	2. se
1. Se	None	None
2. se	2	None

Matings		Children	
Type	Frequency	Possible	Impossible
Se x Se	0.5740	Both	Neither
Se x se	0.3672	Both	Neither
se x se	0.0588	se	Se

It can be seen, from the fact that the only mating from which an exclusion is possible comprises only a little over 5% of all matings, that at this level of testing. If and when it is possible to distinguish between the homozygote and the heterozygote, then, as usual, the position will be improved slightly. The position will then be as follows:

Mother	Child		
	1 SeSe	2 Sese	3 sese
1. SeSe	3	1	All
2. Sese	3	None	1
3. sese	All	3	1

Matings		Children	
Type	Frequency	Possible	Impossible
SeSe x SeSe	0.0664	SeSe	Sese, sese
SeSe x Sese	0.2576	SeSe, Sese	sese
Sese x Sese	0.2500	All	None
SeSe x sese	0.1248	Sese	SeSe, sese
Sese x sese	0.2424	Sese, sese	SeSe
sese x sese	0.0588	sese	SeSe, Sese

THE LEWIS SYSTEM

There seems to be little point in attempting to construct exclusionary tables for the Lewis system at the moment. Since there is no agreement as to the mode of inheritance the system obviously cannot be used as an exclusionary criterion at the moment, and any tables constructed would be purely tentative and of no real value.

Haptoglobin Groups

Although these are not yet extensively used for forensic purposes it is perhaps worthwhile to set out the position which will arise when and if they are so used.

Hp. group of mother	Hp. group of child		
	1. Hp^1/Hp^1	2. Hp^1/Hp^2	3. Hp^2/Hp^2
1. Hp^1/Hp^1	3	1	All
2. Hp^1/Hp^2	3	None	1
3. Hp^2/Hp^2	All	3	1

Further assuming that we may take the Swedish distribution figures as representative, the above information may be cast into the alternative form as follows:-

Matings		Children	
Type	Frequency	Possible	Impossible
$Hp^1/Hp^1 \times Hp^1/Hp^1$	0.0264	Hp^1/Hp^1	$Hp^1/Hp^2, Hp^2/Hp^2$
$Hp^1/Hp^1 \times Hp^1/Hp^2$	0.1536	$Hp^1/Hp^1, Hp^1/Hp^2$	Hp^2/Hp^2
$Hp^1/Hp^1 \times Hp^2/Hp^2$	0.1157	Hp^1/Hp^2	$Hp^1/Hp^1, Hp^2/Hp^2$
$Hp^1/Hp^2 \times Hp^1/Hp^2$	0.2315	All	None
$Hp^1/Hp^2 \times Hp^2/Hp^2$	0.3430	$Hp^1/Hp^2, Hp^2/Hp^2$	Hp^1/Hp^1
$Hp^2/Hp^2 \times Hp^2/Hp^2$	0.1270	Hp^2/Hp^2	$Hp^1/Hp^1, Hp^1/Hp^2$

It may be added that there appears to be no justification, at this stage, for compiling exclusion tables for the Gm and abnormal haemoglobin groups, as insufficient information appears to be available regarding their forensic applications.

GENERAL CONSIDERATIONS

It should perhaps be emphasised that the use of blood tests is not confined to bastardy or affiliation proceedings as such. They can be used in any type of proceeding in which the issue of parentage is raised. In addition to affiliation proceedings as such, suits for nullity on the ground that the woman was pregnant by some other man at the time of the marriage and suits for divorce on the ground of adultery. They can also be used in those cases in which babies have accidentally been interchanged in a maternity hospital and doubt arises as to which child belongs to which set of parents.

A further, and unusual, application of these tests is mentioned by Sussman (1958). He refers to the use of blood testing in applications for derivative citizenship in America. It appears that children of Chinese parents were claiming American citizenship on the basis of their parents' citizenship. The large number of such claims was suspicious and blood grouping was introduced, the applicant children being tested in Hong Kong and the parents in America. As a result 40% of the applications were refused as the tests showed that paternity was excluded. By this means there was exposed an immense "immigration ring" the organisers of which, for doubtless a substantial consideration, provided the necessary contacts and documents to enable Chinese communist refugees to enter America under cover of "derivative citizenship."

MEDICO-LEGAL APPLICATIONS OF BLOOD-GROUP TESTING TO PROBLEMS OF IDENTITY

There is really very little that need be said, at this stage, regarding these problems. The problem is that of testing the blood of a given person and comparing his group with that of a blood stain alleged to have derived from his blood. The most obvious application of these techniques are in criminal trials for homicide. The blood group of blood stains on the prisoner's clothing can be compared with that of his alleged victim, or the blood group of blood stains alleged to have been left at the scene of the crime by the murderer can be compared with that of the prisoner.

The problem in these cases is that of straight comparison of two types of blood. No question of inheritance is involved and no exclusion tables can be drawn up. The only problems that arise in these cases turn on the question of the value that can be attached to evidence of blood grouping in these circumstances. This is a matter which will be considered later.

A very good example of the operation of blood group testing under these circumstances is provided by a case reported by Harley (1944). In this case a mother found blood stains on a mattress in the family's weekend cottage. Her son had recently spent a weekend at the cottage with a male friend, and on discovering the blood stains she adcused her son of homo-sexuality. Her husband thereupon stated that he had cut his hand some weeks previously when he was handling the mattress, and presumed that the blood stains had come from him. At his instructions blood grouping tests were carried out. It was found that the blood stains were of group B, that the son was group O and the father was of group B. It followed that the blood stain could not have come from the son, but could have come from the father.

This determination did not, of course, prove the father's story, but it supplied sufficient probability which may be presumed to have satisfied the very suspicious mother.

Tests of a similar type may also be applied to saliva stains. Cigarette butts left at the scene of the crime can be tested and a determination made as to whether the person who smoked them was a secretor or not, and if so his ABH grouping. Such determinations can be used in the same way as a criterion for determining the probability of the story told by witnesses or accused.

Exactly the same type of testing can be applied to seminal stains. Thus in cases involving carnal knowledge grouping tests can be applied to seminal stains found on the victims garments and to the semen of the accused, and in suitable cases the accused may be excluded.

The possible applications of blood group tests within this general field is limited by little other than the imagination of the writer, and there is little point in continuing to elaborate all possible circumstances in which blood groups could be applied. The principles are exactly the same as those considered above.

THE POSITION OF BLOOD-GROUP TESTS AS EVIDENCE

The first problem that inevitably arises under this head is whether the results of blood group tests are admissible as evidence at all in a court of law. Fortunately there is little that needs to be said on this score at this time. Shortly after the introduction of blood tests doubts were raised as to whether the technique was sufficiently reliable to warrant a court admitting the results of such tests as evidence, but the day appears to be past when it could be asserted, as a general proposition, that, because of the unreliability of the technique, the results of blood group testing cannot be admitted as evidence in a court of law. Thus in the State v. Damm (1937) on rehearing, the court stated:

> "We therefore say, without further elaboration or discussion, that it is our considered opinion that the reliability of the blood test is definitely, and indeed, unanimously established as a matter of expert scientific opinion entertained by authorities in the field, and we think the time has undoubtedly arrived when the result of such tests, made by competant persons and properly offered in evidence should be deemed admissible in a court of justice whenever paternity is in issue."

Neither the English, nor the Australian cases reveal any doubt on this score, and the opinion of Binney J. in Hobson v. Hobson has been quoted earlier.

A second general problem raises the question whether the courts are required to take judicial notice of the nature of the evidence which is submitted in such cases. That they should do so was denied in one American case, Commonwealth v. English (1936) in which the court stated:

> "The record is entirely devoid of proof as to the scientific accuracy of such test. We have only the assertions of counsel in argument and references to certain scientific discussions. The blood-grouping tests have not attained such standing as to justify a court in taking judicial notice of their value."

Later American decisions, however, have not followed this view. In re Swann (1936) the court stated:

> "It is, however, no straining of the doctrine of judicial notice for a particular tribunal to affirm its awareness of the principle underlying such examinations is that certain characteristics or properties of the blood of a parent perpetuate themselves in that of his or her offspring in accordance with the Mendelian Law, and that the results of such tests are, therefore, potentially relevant in the determination of whether a given child is the offspring of specified adults, or vice versa, whether a given adult is the mother or father of a particular child."

In Shanks v. Shanks (1945) the court merely stated:

"Blood types are matters of common or ordinary knowledge"

This point appears not to have been discussed, in so many terms, in either the English or Australia cases, but the assumption has clearly been that judicial notice may be taken of the nature and value of the tests.

So far we have only discussed this problem in purely general terms. We must now consider the various types of proceedings in which blood group evidence may be tendered in more detail, and at the very outset it is necessary to draw attention to the distinction between those cases in which parentage is in dispute and those cases which involve such matters as the identification of stains and the like.

If we consider first the problem of parentage we must stress at the outset the fact that the use of blood group testing can only exclude paternity, it can never prove it. The results can show that a given man cannot be the father of the child, but they cannot show that he is the father, the most that they could do would be to show that he could be the father. This distinction is important when we consider the evidential problems raised by these tests. Supposing that, in an affiliation suit, the parties have voluntarily submitted to blood tests. If the results indicate that the defendant could not be the father of the child then no one doubts that the

evidence is admissible. What, however, is the position if the results do not exclude him from paternity? Can the mother claim to adduce the results as evidence supporting her claim. On this point there is considerable confusion. The trend of American decisions, for the problem does not seem to have come before the Australian or English courts, seems to be against the admissibility of such evidence. Thus in State v. Morris (1951) and People v. Nichols (1954) it was held that blood test results showing possible paternity were of no probative value and should have been excluded as irrelevant.

If, however, we turn to consider those cases concerned with the identification of stains and the like, we find that a rather different principle seems to be applied. This principle, as enunciated in Shanks v. Shanks is that:

> "the objection of remoteness goes to the weight of the evidence rather than to its admissibility. To exclude evidence merely because it tends to establish a possibility, rather than a probability, would produce curious results not heretofore thought of."

Again, in Williams v. State (1940) the court stated:

> "any evidence tending to indentify defendant as the guilty person and to show his presence at the scene of the crime is relevant and competant."

This was a case in which the accused was charged with rape. The evidence was that blood found on the coat of the accused was of the same group as that of the victim, namely group O. The defence objected that 45% of the population are group O and that therefore the evidence was not probative. The submission the court overruled on the ground stated above. A similar conclusion was reached in the case of Commonwealth v. Stratti (1950) which involved similar facts.

It is submitted that, in principle, there is very little difference between the two types of cases and that the principle enunciated in Shanks v. Shanks should, in theory at least, be applicable in affiliation suits, i.e., the evidence should be regarded as admissible, although the weight to be attached to it remains a problem in each particular case. The finding that both the stain and victim are of group O whilst the accused's own blood is of some other group is not necessarily very weighty evidence. On the other hand a finding that both the stain and the victim were B, NS, $C^{w}D^{u}c$/cde, Lu(a-), K could be regarded as very cogent evidence indeed since, outside the family of the victim there would not be another man in ten millions. This is not proof positive, but it is certainly very weighty evidence indeed.

It is perhaps worth emphasising that in criminal cases involving stain identification the weight of blood group evidence may be considerably increased, not because of factors related to the tests themselves but owing to the way in which the evidence is used. The tests may be used as a check upon the veracity of explanations given by the prisoner. Thus if we consider the situation which arose in Shanks v. Shanks. Upon finding blood stains on the coat of the accused the police would presumably ask for an explanation. The accused might well reply that he cut himself whilst shaving. If blood tests then showed that the blood stain and the victim were of group O and the accused of group A then the test have proved almost exclusively that the accused is lying, without of course proving that the blood stains are those from the victim. In circumstances such as these the tests, although not necessarily of great probative value as regards the identification of the source of the stain, are almost conclusive

as regards the truth of the explanation provided.

Even in paternity suits the situation may be such that the tests may achieve high probative value even of positive paternity. Thus the situation may be such that there are only two men who have to be considered as possible fathers blood tests by excluding one will then be cogent evidence for the paternity of the other, even though blood tests on the latter's own blood may be indecisive.

Despite the American decisions considered above we would submit that in all cases blood group evidence should be considered as admissible evidence, although the weight to be attached to that evidence will depend upon the facts of the particular case. As mentioned above, there is no discussion of this problem in the English or Australian reports, but our submission would seem to be consistent with an anonymous case reported in the Justice of the Peace and Local Government Review for 1935. In this case a woman in a maintenance suit to adduce blood group evidence that the man from who she was claiming could have been the father of her child as corroborative evidence of her claim. The justices refused to accept this as sufficient corroboration. The report is very brief but the implication is that the evidence was not rejected as inadmissible but held to be insufficient corroboration on the ground that it merely showed that the defendant, along with some million or so other men, could have been the father. This we would respectfully submit is the correct approach to these problems.

We must now turn to consider the other main evidential problem raised by blood group testing, namely, the weight to be attached to such evidence when it purports to establish an exclusion of paternity or as the source of a stain.

There is a tendency in some non-medical literature on the subject to lay undue stress on reported incidents which might seem to weaken belief in the reliability of the tests. This, we would submit, is a mistaken attitude. The real problem is not, what is the absolute accuracy of blood tests, but rather how much more or less accurate are they than the traditional methods of adducing proof.[1] That is to say we should really be concerned with their relative accuracy rather than with their absolute accuracy.

Clearly, however, some measure of absolute accuracy is necessary before comparison is possible, and so we may briefly consider the techniques of blood testing in order to assesstheir accuracy, or what Professor Ross has called their biological accuracy. Into the details of the various techniques employed we are not competant to go, and it will be sufficient to quote here the view of Andresen (1952) that

> "blood group determination is one of the most accurate biological methods."

The possibility of human error always remains, of course, although with suitable controls the risk of error can be reduced to a minimum. It is difficult to obtain any sort of statistical measure of the incidence of human error, but it would be foolish to deny that the possibility exists.

A second factor which must also be considered when discussing the evidential value of blood tests, is the constancy of the blood grouping of an individual. Particularly as applied in disputed paternity proceedings, blood group testing assumes that an individual's blood group remains unchanged throughout his life, and indeed that it is established in the child either at, or, at the very latest, within a short time of birth. With regard to the latter point we have shown that, in relation to each

of the individual blood groups, the antigens are well developed in most cases well before birth. It may perhaps be added that the establishment of the time at which the blood grouping of a foetus may be determined could have important medico-legal applications in cases, for example, in which child destruction or concealment of birth are involved and it is necessary to establish a relationship between the foetus and the woman who has been charged. In such cases blood group determinations could, in certain circumstances play a useful part.

With regard to the constancy of an individual's blood group, it is of course difficult to show that blood groups do remain unchanged throughout life, and indeed there are cases in which disease seems to affect in some way the apparent grouping of an individual. The case reported by van Loghem et al. (1957) and that reported by Stratton et al. (1958) show that absolute constancy cannot be assumed, yet it appears to be true that no case of a change has ever been reported in the case of a normal healthy adult.

It should perhaps be added that the reported "transformation" of the Lewis groups of red cells are only apparent exceptions. That is to say they are only exceptions in so far as the Lewis system is thought of as an antigenic system. Once the concept of the system as a secretor system is adopted the apparent exceptions disappear.

Thus on the score of the constancy of the blood group systems, the evidential value of blood group testing remains high. The constancy is not absolute but all the real exceptions appear to be associated with well recognised blood diseases, so that the chance of an error on this score can be reduced by suitable checks for the existence of these diseases.

Finally, and as applied in disputed paternity proceedings, there remains the problem of the accuracy of the theories of inheritance which have been worked out. Given a wrong theory of inheritance and exclusions based thereon will be valueless. It will be remembered that from 1910 to 1924 the inheritance of the ABO system was thought to be based upon the existence of two independent pairs of allelomorphs, and it was not until Bernstein produced his theory in 1924, a theory which has now stood for 35 years in the face of intense blood group testing, that the ABO system was put on what must now be regarded as the right lines. It may be added that it seems unlikely that the theory of von Dungern and Hirszfeld was ever extensively employed in any court cases, for the first case in which blood group evidence was adduced in a paternity case was heard by the German courts in 1924, the year in which Bernstein first announced his triple allelomorph theory.

The same is true of the Lewis system. The original theory that Le(a-) was inherited as a Mendelian recessive has subsequently been shown to be fundamentally incorrect. It is notable, however, and a commentary upon the pace of serological research, that whilst it took fourteen years to establish that the von Dungern Hirszfeld theory for the ABO system was incorrect, it took barely two years to show that the original theory proposed for the Lewis system was incorrect.

The only check on the accuracy of the inheritance theories is that of statistical control based on very large numbers of tests. Given large enough numbers it is most unlikely that any error in the inheritance theory

will remain undetected for very long. Once a theory has withstood several years of intensive testing involving large numbers with no proved exceptions it may be regarded as "established". It may be remarked in this context that, so far as we are aware, no one has ever proved positively that it is impossible for two persons to have the same fingerprints. The acceptance of finger-prints rests simply on the fact that no cases of identical finger-prints have ever been observed, although the number of prints taken must be astronomical. No court would, today, pay much attention to counsel who endeavoured to argue that the individuality of finger-prints had not been conclusively established, and in our submission they should adopt the same attitude to counsel who argue that the inheritance system of the major blood groups has not been established. There is, of course, always the difficulty of deciding when a working hypothesis acquires the status of an established theory. The only criterion that can be adopted here is one of statistical control, namely, when the number of tested families becomes large enough. Once this somewhat arbitrary Rubicon is crossed the hypothesis may be regarded as an established theory. In the case of the Lewis system the total number of families examined by 1957, and relating to which the results were published was only 723, whilst by 1954 the total number of samples tested throughout the world was only a little over 10,000. This number was clearly insufficient, in this particular case, to afford a guarantee of the accuracy of the theory.

It is difficult to gather accurate statistics as to the number of tests and family studies that had been done in the ABO system prior to 1910 (the date of the von Dungern and Hirszfeld theory) and prior to 1924 (the

date of the Bernstein theory). So far as Europe is concerned Mourant (1958) lists only one series prior to 1910, that of Decastello and Sturli in 1902 (although our search was confined to those with a date as listed and does not include figures quoted as having been taken from a publication by a person other than the original author). It may also be added that von Dungern and Hirszfeld, in their original paper, based their theory on tests on 72 families.

Even assuming, however, that a given theory of inheritance is regarded as established there remains the difficulty of mutations. The possibility of a mutation means that there is always the chance of a genuine exception to any theory of inheritance. The possibility of a mutation, however, is very low indeed - earlier we quoted the opinion of Ford that a mutation rate of 1 in 50,000 is "exceptionally high and rarely exceeded". At least one case, however, has been reported in which a genuine mutation appears to have occurred. This is the well known case reported by Haselhorst and Lauer (1930, 1931) in which the child of a A_2B mother was found to be of group O. The child was, however, a blind deaf mute with gross congenital deformities. A similar exception was also reported by Kossovitch (1929). Very careful testing is clearly necessary before it can be accepted that a mutation has occurred. This is illustrated by the case reported by Worsaae (1930) in which an A_2B mother produced a group O child. It was later found that the child possessed a weak A_2 antigen. The existence of very weak sub-groups within the ABO system always presents a difficulty in these cases. This is illustrated by the case reported by Witebsky and Young (1945) in which parents of groups B and A_2B produced a child who was grouped as A_3B.

"Exceptions" of this kind are always possible although as research proceeds they are likely to lose their exceptional character. Cases involving the Xx inhibitor genes might well have been put down as "exceptions" a few years ago, and if an issue of paternity had arisen in such a case an inaccurate exclusion might well have resulted. Again, in the Rh system, Henningsen (1958) has reported a case in which maternity would have been excluded in a paternity case had not the rare chromosome -D- been remembered. The same applies in the case of the M^g antigen which we discussed earlier in which paternity would have been excluded if anti-M and anti-N had been used alone.

Another rare occurrence, which could lead to incorrect results is the existence of blood group chimeras. These are twins in which, owing to uterine vascular anastomosis, interchange of primitive erythrocytes takes place so that each twin possesses two types of red cells. The first example of this phenomenon in man was reported by Dunsford et al. (1953) since when at least two other cases have been reported.

Factors such as these reduce the "biological certainty" of blood group exclusions to a little below 100%, but the fact remains that the certainty of such tests remains very high. Some indication of the degree of certainty attainable can be gathered from the report of the Inter-Scandanavian Meeting on Genetics and Legal Medicine (1952) who reported that the degree of certainty of the ABO system was 99.99% i.e., a risk of error of 1 in 10,000.

It should be remarked, in passing, that the reliability of the various blood group systems is not uniform. Thus the Inter-Scandanavian Meeting on Genetics and Legal Medicine (1952) gave the certainty of the MN system as being only 99.9% accurate, i.e. a risk of error of 1 in 1,000. The authorities however, seem to differ as to which of the various systems are sufficiently reliable and well established to warrant their use in paternity cases.

The Committee on Medico-Legal Problems of the American Medical Association, reporting in 1956, recommend against the use of the sub-groups of the ABO system:

> "Tests for the sub-groups of A are not sufficiently reliable for medico-legal use. The serologic distinction between agglutinins A_1 and A_2 is not sharp, so that the diagnosis is not infrequently difficult to make, especially in newborn babies and individuals of group AB. Moreover, intermediate forms exist between A_1 and A_2. At any rate the chances of excluding paternity for a falsely accused man, which is about 18.5% using factors A and B, would be increased by only 1 or 2% were the subgroups of A applied. Therefore this committee finds that the subgroups of A remain too unreliable for general medico-legal use."

The attitude of the Danish Medico-Legal Council (1947) is slightly more favourable. They state that "the possibility of paternity incompatible with the $A_1 - A_2$ system has to be considered very remote" but they add:

> "until greater experience is gained in this matter, this paternity will not be considered so improbable that it will be looked upon as safe to attach a decisive importance to the outcome of the blood typing in such cases."

In this connection it may also be noted that Andresen (1952) points out that the sub-groups of A tend to be particularly unreliable in the newborn, and he recommends further testing after a year in those cases in which the subgroup is of importance.

Although there is general agreement on the use of the MN system, the value that can be attached to the use of S and s is uncertain. The American Medical Association report as follows:

> "the number of studies to date on the factor S is small, because of the scarcity of this reagent, which unlike anti-M and anti-N cannot, at present, be produced at will. Therefore, the medico-legal application of the S test should be limited to selected cases and exclusions of paternity based on this test alone should be qualified by pointing out that the statistical basis of this test is still incomplete, though there is no reason to doubt its reliability. Reagents for anti-s are even rarer than anti-S. Moreover, the anti-s reagents available up to the present had to be used with the anti-globulin technique, and the results were reproducible only with difficulty. For these reasons, the medico-legal application of factor s is not recommended for the present."

We have been unable to find any other published views regarding the use of Ss, but it would appear to the writer, approaching the matter as a layman, that the attitude of the American Medical Association tends towards over abundant caution.

So far as the Rh system is concerned the American Medical Association recommend that tests be limited to Rh_o, rh', rh'' and hr', which being translated are C,D,E and c, this being the level of testing contemplated in the last of the exclusion tables for the Rh system which we compiled and which were quoted earlier.

The position of the P system is doubtful. The American Medical Association recommend against its use, but the system has on occasion been used in Denmark and Sweden.

None of the other systems has yet received the approval of the American Medical Association for general use in paternity cases, and there are few reports concerning their use.

There would appear to be in some writers, confusion as to the nature of the accuracy of the laws of inheritance as used in blood group testing. This confusion is well illustrated by the recent article by Professor Ross, Professor of Jurisprudence in the University of Copenhagen. In his article on The Value of Blood Tests as Evidence in Paternity Cases (1958), Professor Ross draws a distinction between "prospective" and "retrospective" laws of inheritance. The former he defines as those which

> "presuppose that the qualities which the parents possess are known and on this basis the rules declare what quality progeny will have."

whilst the latter he defines as:

> "(those which) declare retrospectively, with reference to the rules of inheritance and other factors, who (probably) could possibly (sic) be the father of the child."

Having drawn this distinction, Professor Ross emphasises that it is the retrospective laws, as he has defined them, which are relevant so far as the application of blood group tests in paternity cases are concerned. He further emphasises that whatever may be the probability of the prospective laws, the same probability does not attach to the equivalent retrospective law.

We would submit, with respect, that this analysis of the position overlooks the exclusionary nature of the criterion obtained by applying blood group testing. The point may be illustrated by a simple example. Consider the case of a group A child born to a group O mother. By the laws of Mendelian genetics, as applied to blood groups, it can be shown, that the father of the child must be either group A or group AB. The mere fact, however, that the alleged father is of group AB does not established that he is in fact the father; it merely establishes that he

could be the father - but so could any other man of group AB (or of group A). On the other hand, if the alleged father turns out to be of group B then it can be said that he could not be the father of that child. So far as the evidential value of blood tests is concerned, it is the certainty of the exclusionary rules which is the relevant consideration, and in so far as the ABO system is concerned we may accept the figure of 99.99% as the certainty of the system. This figure, however, may be applied to the rule whether couched in prospective or retrospective form. Thus one may consider the position arising in the case of an O x AB mating. The offspring of such a mating must be of group A or group B, but cannot be groups O or AB. Therefore given the blood groups of the parents, the exclusionary rule stated in a prospective form is that the parents of groups O and AB cannot have children of groups O or AB, and this rule may be said to have a certainty of 99.99%. On the other hand the same rule may be stated in retrospective form without in any way affecting the risk of error involved. Thus given a group A child and a group O mother, the rule that the father could not be group B (or that he must be groups A or AB) still has a probability of 99.99% for the two factors underlying the risk of error are the same in both cases.

If however we consider the rules of inheritance, as defined by Professor Ross, then clearly his distinction between prospective and retrospective rules becomes valid, although not strictly applicable to the problem of the application of blood groups in paternity suits. Given the blood groups of the parents as O and AB then it can be seen that their chances of having a group A child is approximately 50% (as is their chance of having a group B child) so that the prospective law

which states that parents of groups O and AB will have a group A child has approximately 50% validity. If we consider the situation retrospectively, however, that is to say, given the blood group of the mother as O and that of the child as A then the probability that the father will be of group AB will depend on two factors:

a) the number of other blood groups that the father could biologically posses

b) the frequency of distribution of the relevant groups

The father of a group A child born of a group O mother could biologically be group AB or group A (but could not be group O or B). Taking the Australian figures for the distribution of the ABO groups, we see that the frequency of occurrence of group A is 39.75 and that of group AB is 2.97. so that the chances of the father being of group AB are a little under 7%.

This type of consideration, however, is irrelevant when discussing the application of blood groups to disputed paternity cases. In such cases the only relevant rules are those of an exclusionary nature and their degree of certainty depends only upon the chances of human error, the possibility of a mutation and the chances of the operation of unknown factors all of which could lead to a wrong determination, but the combined effect of all these factors would hardly add up to a risk of error of more than 1 in 100 to put it at its very highest, and in many cases it would be a good deal lower than this since where paternity is excluded by more than one system the possibility of an error occurring in both systems at the same time is very low indeed.

Having considered the various factors which affect the reliability of blood group determinations we must now turn to assess their relative merits in comparison with the traditional ways of adducing evidence.

It is, of course, virtually impossible to obtain any sort of rational estimate as to the accuracy of the traditional methods. Just how accurate a judge is when he listens to the parties in court and tries to determine who is speaking the truth is a matter which lies almost outside the realms of rational enquiry. There is, however, one line of enquiry which could lead to something like a reasonable estimate of the accuracy of the traditional methods. This is a line which we are unfortunately unable to pursue here, but it may be thought worth while to outline the basic method which could be employed.

The method turns upon the fact that it is possible to calculate the statistical probability of a man being excluded from paternity, when such a charge is falsely brought against him, by the application of the known blood groups. The chances of an exclusion by any given system may be illustrated by taking a simple case such as that presented by the Lutheran system. Here the only mating from which an exclusion is possible is a Lu(a-) x Lu(a-) mating, and in this case only an Lu(a+) child would enable an exclusion to be made. The frequency of such a mating is 0.8529 whilst the chance of the real father of the child carrying the Lu^a gene is 0.0390 which is the frequency of the Lu^a gene. It follows that the chances of an exclusion from the Lutheran system is 0.8529 x 0.0390 which is 0.03327.

In connection with the problem of determination of the "efficiency" of a blood group system, it is worth mentioning that Professor Sir Ronald Fisher has provided a series of standard calculations for evaluating blood group systems. He distinguishes between four types of problem, namely,

a) "doubtful identity - how frequently will different persons (supposedly unrelated) be of the same phenotype?

b) identical twins - how frequently will fraternal twins, children of the same father, be of the same phenotype?

c) doubtful parentage - if an infant is interchanged with another in a maternity hospital, how frequently will the supposed child be of a phenotype compatible with those of its supposed parents?

c) disputed paternity - how frequently will the child of another man be compatible with falsely accepted paternity?"

However, to each question, each of the phenotypes will return a different answer, and Fisher introduces the concept of the power of a system as a whole, i.e., the proportion of all cases which present themselves, in which testing the parties for a given blood group system, will fail to make a discrimination. The power of a system is not the probability itself of a failure to discriminate, but, if this probability is represented by P, is

$$-\log P = \log (1/P)$$

Considering the problem of identity and using the MNSs system as a model Fisher sets out the power of the system as follows: Taking the frequencies of the gene combinations from Race and Sanger (1947) he obtains the following table for the genotypic and phenotypic frequencies:

Genotypes	Frequencies %	Phenotypes with anti-s		Phenotypes without anti-s	
MS/MS	6.1094	MS	6.1094	MS	20.1058
MS/Ms	13.9964	MSs	13.9964		
Ms/Ms	8.0163	Ms	8.0163	Ms	8.0163
MS/NS	3.9650	MNS	3.9650	MNS	27.7611
MS/Ns	19.2542	MNSs	23.7961		
Ms/NS	4.5419				
Ms/Ns	22.0553	MNs	22.0553	MNs	22.0553
NS/NS	0.6433	NS	0.6433	NS	6.8913
NS/Ns	5.2480	NSs	6.2480		
Ns/Ns	15.1702	Ns	15.1702	Ns	15.1702

From these values the probability of a failure to discriminate, in the case of identity, can be obtained. Thus given an individual of MS phenotype, then the probability of the blood of another individual being also MS will be 0.201058 (using three antisera) or 0.061094 (using four antisera). The probability of the system as a whole failing to discriminate can be taken as the sum of the squares of the phenotypic frequencies. This gives the results shown in the following table:

	3 antisera	4 antisera
Probability of non-discrimination	0.200324	0.163548
Power log (1/P)	1.60783	1.31066
Power per cent	100	112.6

Thus it can be seen that the use of anti-s increases the power of the system, in cases of identity by 12.6%.

The same type of analysis can be applied to cases of infant interchange and disputed paternity. For these cases, assuming the use of three antisera the usual 6 x 6 table is compiled in each cell of which is entered the sum of the frequencies of all the phenotypes which each mating could produce. This gives the following table:

Frequency	Phenotype of mother	Phenotype of father							
		MS	Ms	MNS	MNs	NS	Ns		
20.1058	MS	28.1221	28.1221	77.9385	77.9385	49.8164	49.8164	57.7245	74.0642
8.0163	Ms	28.1221	8.0163	77.9385	30.0716	49.8164	22.0553	41.3446	53.0477
27.7611	MNS	77.9385	77.9385	100.0000	100.0000	71.8779	71.8779	87.5917	87.5917
22.0533	MNs	77.9385	30.0716	100.0000	45.2418	71.8779	37.2255	66.4206	66.4206
6.8913	NS	49.8164	49.8164	71.8779	71.8779	22.0615	22.0615	54.6835	76.0783
15.1702	Ns	49.8164	22.0553	71.8779	37.2255	22.0615	15.1702	43.7700	60.8949

Sir Ronald Fisher's directions are then as follows:

Multiplying each column by the paternal frequency then by addition the first column on the right in the above table is obtained. If these values are then multiplied by the maternal frequencies the general average of 64.2944% is obtained which is the frequency with which three antisera will fail to detect an interchange.

In cases of disputed paternity the values in the above table should be divided by the sum of the frequencies of the phenotypes which might have been born to the mother without restriction as to paternity. These are in fact the values in the column headed MNS, and from these figures the percentages of wrongly ascribed paternity which the use of the three antisera would not disprove can be obtained. These are shown in the second column on the right, their average being 72.5900% i.e. in a little over a quarter of cases presented would a successful exclusion of paternity be possible.

Using this type of analysis Fisher is able to compare the power of the system within three antisera with its power when four antisera are used. He tabulates his results as follows:

	3 antisera	4 antisera	% increase in power
Identity	1.60783	1.81066	12.6
Twins	0.72792	0.81471	11.9
Interchange	0.44170	0.60973	38.0
Paternity	0.32035	0.40263	25.7

It is not without interest to observe that the use of anti-s gives a 25% increase in power when the MNSs system is applied to paternity problems. This type of analysis is of considerable value in that it indicates the improvement which can be expected from the use of additional anti-bodies.

Boyd (1955) has a slightly different approach to this problem. His calculations are as follows:

Let a = the frequency of MS
b = " " " NS
c = " " " Ms
d = " " " Ns

and let

m = a + c
n = b + d
p = a + b
q = c + d

then the chances of an exclusion using three antisera will be

$P_{MS} = n(1 - mn)$

$P_{M} = n(1 - mn) + aq^2 + bcd$

$P_{MNS} = 0$

$P_{MN} = pq^2$

$P_{NS} = m(1 - mn)$

$P_{M,N,S} = mn(1 - mn) + (ac^2 + bd^2)q^2 + 2cdpq^2 + cd(ad^2 + bc^2)$

$P_{N} = m(1 - mn) + bq^2 + acd$

where P_{MS} = the chance of excluding a man of group MS etc., and $P_{M,N,S}$ = the chance of excluding a man of unknown MNS grouping. Using the MNS frequency distribution figures for England given by Race and Sanger, Boyd calculates the chances of excluding paternity in the MNS system as follows:

MS	0.3527
M	0.4734
MNS	0.0000
MN	0.1481
NS	0.3932
N	0.4618
unknown	0.2390

This figure, 0.2390, compares with 0.3158 obtained by the use of four antisera, as calculated by Wiener.

The calculations in the case of the Rh system are rather complex. Professor Sir Ronald Fisher prepared a table which was printed in the earlier editions of Race and Sanger but without any indications of the method upon which it was constructed. It is reproduced below as Table I. Boyd, however, has produced a general method for calculating the chances of an exclusion which is as follows. He first constructs a table showing the frequency with which children of the various phenotypes would be born to women of the various phenotypes when mated with men drawn at random from the population. This is done by considering the children which would be born to women of each phenotype when they receive Rh genes in numbers proportional to the gene frequency of the population as a whole. This is reproduced below as Table II.

Taking the gene frequencies to be:

$R_2 = t = 0.1280$

$R_0 = u = 0.0305$

$R'' = v = 0.0170$

$r = w = 0.3790$

$R_z = x = 0.0013$

$R_1 = y = 0.4361$

$R' = z = 0.0081$

then the frequency of the various phenotypes will be as follows:

cde	w^2
cdE	$v^2 + 2vw$
cDe	$u^2 + 2xw$
cDE	$t^2 + 2tv + 2\,tu + 2\,tw + 2\,uv$
Cde/c	$2wz$
CdE/c	$2vz$
CDe/c	$2(uy + wy + uz)$
CDE/c	$2(tx + ty + tz + vx + vy + ux + wx)$
Cde/C	z^2
CdE/C	Absent
CDe/C	$y^2 + 2yz$
CDE/C	$x^2 + 2xy + 2xz$

Substituting the gene frequency figures in the above equations and then substituting the values thus obtained in Table II we obtain Table III. Since to derive general algebraic formulae expressing the possibility of an exclusion from the normal standard exclusion involves arduous algebraic manipulations Boyd constructs a table from the formulae of Table II based on the actual gene frequency figures, which is shown below as Table IV. This is constructed by adding, from Table III, using a standard exclusion table as a guide, for a man of a given phenotype all children's frequencies which, for each type of mother, exclude paternity. The chances of an exclusion are thus seen to be 25% using the four antisera implied in the above tables. It may be added that Allen, Jones and Diamond (1954) have calculated that, using seven antisera, namely, anti-C, anti-C^W, anti-c, anti-D, anti-E, anti-e and anti-f the chances of an exclusion would rise to 35%.

TABLE I

Frequency of Failure to Discriminate Respectively Parentage and Paternity Based on Approximate Gene Frequencies (Fisher, 1944)

Phenotype of father	Phenotype of Mother: R_2	R_1R_2	R_1R_z	$R''r$	$R'R''$	$R'R_y$	R_or	R_1r	R_1R_1	rr	$R'r$	$R'R'$	Parentage	Paternity
	.1519	.1426	.0083	.0081	.0002	0	.0164	.3364	.1680	.1600	.0080	.0001		All women
R_2	.3364	.8236	.4872	.3364	.8236	.4872	.3364	.8236	.4872	.3364	.8236	.4872	.6004	
	.58	.79	.58	.58	.79	.58	.58	.79	.58	.58	.79	.58		.6823
R_1R_2	.8236	1.0000	.6636	.8236	1.0000	.6636	.8236	1.0000	.6636	.8236	1.0000	.6636	.8813	
	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.0000
R_1R_z	.4872	.6636	.1764	.4872	.6636	.1764	.4872	.6636	.1764	.4872	.6636	.1764	.5183	
	.42	.71	.42	.42	.71	.42	.42	.71	.42	.42	.71	.42		.5613
$R''r$	.3364	.8236	.4872	.1681	.1763	.0082	.3364	.8236	.4872	.1681	.1763	.0082	.5667	
	.58	.79	.58	.41	.415	.41	.58	.79	.58	.41	.415	.41		.6506
$R'R''$	.8236	1.0000	.6636	.1763	.1764	.0083	.8236	1.0000	.6636	.1763	.1764	.0083	.7657	
	1.00	1.00	1.00	.42	.42	.42	1.00	1.00	1.00	.42	.42	.42		.8977
$R'R_y$	.4872	.6636	.1764	.0082	.0083	.0001	.4872	.6636	.1764	.0082	.0083	.0001	.4324	
	.42	.71	.42	.01	.215	.01	.42	.71	.42	.01	.215	.01		.4883
R_or	.3364	.8236	.4872	.3364	.8236	.4872	.1764	.5208	.3444	.1764	.5208	.3444	.4439	
	.58	.79	.58	.58	.79	.58	.42	.625	.42	.42	.625	.42		.5704
R_1r	.8236	1.0000	.6636	.8236	1.0000	.6636	.5208	.6889	.5125	.5208	.6889	.5125	.6954	
	1.00	1.00	1.00	1.00	1.00	1.00	.83	.83	.83	.83	.83	.83		.8829
R_1R_1	.4872	.6636	.1764	.4872	.6636	.1764	.3444	.5125	.1681	.3444	.5125	.1681	.4379	
	.42	.71	.42	.42	.71	.42	.41	.62	.41	.41	.62	.41		.5268
rr	.3364	.8236	.4872	.1681	.1763	.0082	.1764	.5208	.3444	.1600	.1680	.0080	.4369	
	.58	.79	.58	.41	.415	.41	.42	.625	.42	.40	.405	.40		.5640
$R'r$	.8236	1.0000	.6636	.1763	.1764	.0083	.5208	.6889	.5125	.1680	.1681	.0081	.6293	
	1.00	1.00	1.00	.42	.42	.42	.83	.83	.83	.41	.41	.41		.8075
$R'R'$	.4872	.6636	.1764	.0082	.0083	.0001	.3444	.5125	.1681	.0080	.0081	.0001	.3778	
	.42	.71	.42	.01	.215	.01	.41	.62	.41	.01	.21	.01		.4199

Approximate gene frequencies assumed:

R_1	r	R_2	R_o	R'	R''	Rz	Ry	
40	40	15	2	1	1	1	0	per cent

All matings: Parentage .6160; Paternity .7480

TABLE III

Phenotype of Children	Phenotype of Mother										
	cde	cdE	cDe	cDE	Cde/c	CdE/c	CDe/c	CDE/c	Cde/C	CDe/C	CDE/C
1. cde	0.0544	0.0024	0.0044	0.0184	0.0012	—	0.0626	0.0002	—	—	—
2. cdE	0.0024	0.0028	0.00002	0.0019	0.0001	0.0001	0.0028	0.0029	—	—	—
3. cDe	0.0044	0.0002	0.0055	0.0033	0.0001	—	0.0106	0.0000	—	—	—
4. cDE	0.0184	0.0019	0.0033	0.0466	0.0004	0.0000	0.0231	0.0329	—	—	—
5. Cde/c	0.0012	0.0001	0.0001	0.0004	0.0012	0.0001	0.0014	0.0004	0.0000	0.0013	0.0000
6. CdE/c	—	0.0001	—	0.0000	0.0001	0.0000	0.0000	0.0001	0.0000	0.0001	0.0000
7. CDe/c	0.0626	0.0028	0.0106	0.0231	0.0014	0.0000	0.1513	0.0262	0.0000	0.0794	0.0002
8. CDE/c	0.0002	0.0029	0.0000	0.0329	0.0004	0.0001	0.0262	0.0383	0.0000	0.0285	0.0004
9. Cde/C	—	—	—	—	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
10. CDe/C	—	—	—	—	0.0013	0.0001	0.0794	0.0285	0.0000	0.0876	0.0003
11. CDE/C	—	—	—	—	0.0000	0.0000	0.0002	0.0004	0.0000	0.0003	0.0003

TABLE IV

Phenotype	Frequency	Probability
cde	0.1436	0.4495
cdE	0.0131	0.3628
cDe	0.0241	0.4414
cDE	0.1266	0.3355
Cde/c	0.0062	0.1845
CdE/c	0.0003	0.0973
CDe/c	0.3577	0.1066
CDE/c	0.1299	0
Cde/C	0.0001	0.5162
CDe/C	0.1973	0.4448
CDE/C	0.0011	0.4175
Unknown	1.0000	0.2500

The figures given by Race and Sanger (1958) for seven of the systems are as follows:

ABO	0.1760
MNSs	0.2390
Rh	0.2520
Kell	0.0379
Lutheran	0.0333
Duffy	0.0487
Kidd	0.0286

To these figures we may add the chances of an exclusion by the secretor system which would be 0.02985. The chances of an exclusion using any combination of the above groups will be the sum of the chances of using each group separately, so that the chances of an exclusion using all the above systems, including the secretor system will be a little over 60%, i.e. 60% of all men wrongfully accused of paternity could be exonerated by the use of blood group tests.

The actual results of the application of blood tests in disputed paternity proceedings, taken with the above figures provide some measure of the relative degree of truthfulness of women who bring affiliation proceedings. Schiff's results for the years 1924-1934 (excluding 1929) using the ABO system throughout the series, and the MN system from 1931 are as follows. The figure given for the MN system is, of course, lower than that quoted above as Schiff was unable to employ the subdivisions resulting from the discovery of Ss.

Examination for	Chances of excluding	No. tested	Exclusions	
			No.	%
O,A,B	17.60	1822	140	7.7
M,N	18.6	1269	109	8.6
Both	33.0	1129	160	14.2

Thus using both systems 14% of the accused men were proved innocent, but assuming all the accused men to have been innocent one would have expected that one third would have been exonerated so that one may conclude that half of the men tested by Schiff were really "guilty" or, in other words, half of the women were inaccurate in their accusations. Thus some measure is provided for the assessment of the relative truthfulness of women who commence affiliation proceedings.

It may be remarked that the relative truthfulness of women seems not to show the geographical variation of the blood groups themselves. Thus Wiener quotes the figures collected by Levine for the results obtained in Europe up to 1932 which are as follows:

Country	No. of Cases	Exclusions	
		No.	%
Germany (Schiff)	4519	353	7.8
Austria (Werkgartner)	700	63	9.0
Danzig (Püschel)	600	39	6.5
Denmark (Thomsen)	50	6	12.0
Denmark (Sand)	500	64	12.8
Sweden (Wolff)	259	17	6.6
Norway, Switzerland, Lithuania quoted by Schiff	37	4	10.8
Total	6665	546	8.2

Using the ABO system the percentage exclusion, assuming all the men to have been innocent, is expected to be a little over 16%. The average percentage of exclusions actually obtained is a little over 8% so that one may deduce that of the 6665 men examined approximately one half were in fact "guilty" and that therefore one half of the women were lying.

Three other collections of data have been made. Wiener, covering the European results 1930-37 and the English and American results 1932-1942, compiles the following table:

Investigation	No. of Cases	Exclusion			
		ABO	MN	Total	%
Schiff (1933)	911	69	82	139	14.7
Dambrovsky (1938)	691	46	38	76	12.5
Wolff & Jonsson (1935)	600	36	38	69	11.5
Clausen (1934)	119	12	15	25	21.0
Routil (1935)	129	11	10	21	16.3
Püschel(1934)	156	17	17	32	20.5
Hirszfeld	180	9	7	13	7.2
Friedenreich	1778			425	23.9
Harley & Roche-Lynch (1940)	50	4	5	8	16.0
Wiener (1935)	432	27	24	46	10.7
Levine (1939)	81	1	6	7	8.7
Witebsky (1940)	131	8	11	18	13.7
Guttmacher	74	7	3	10	13.5
Evans	133	8	6	14	10.5
Hyman & Snyder (1936)	75	3	10	13	17.3

If the actual results be compared with the percentage of affiliation cases in which the putative husband is rendered liable by a court proceeding without the aid of blood groups then some measure of the accuracy of the traditional methods of dealing with these cases is provided.

Unger (1953) reports a series which would appear to be the first in which the Rh system was employed as well as the ABO and the MN. In 108 cases thirty exclusions were obtained which suggests that the women in this series were a little less truthful than the average. It is perhaps worth noting that of the thirty exclusions only six were excluded by more than one system, none being excluded by all three.

The last series of cases that is worth considering is that reported by Sussman (1956). This series was obtained from the results of applying blood group testing to derivative citizenship applications in the United States, as mentioned earlier. In this series also the Rh system was employed as well as the ABO and MN systems. The results based on a very large number of tests showed 40% of exclusions. Since employment of those three systems gives approximately a fifty per cent chance of obtaining an exclusion the conclusion would appear to be that some 80% of the claims were false. There are clearly, therefore, circumstances in which a higher rate of untruthfulness may be expected than that arising from normal domestic situations.

There is one final problem connected with the evidential value of the results of blood group testing that we have to consider. This relates to the question whether the results of such tests can be considered as conclusive. In considering this problem it is necessary to distinguish between those cases in which the tests result in an exclusion, whether of paternity or as the source of a stain, and those which do not result in an exclusion.

The attitude of the American courts, for once again there is no relevant English or Australian authority, towards the value of evidence which shows an exclusion has undergone a change in recent years. The earlier attitude was that such evidence was not conclusive but could be considered by the court along with such other evidence as may be available. This was the attitude adopted in Arais v. Kalsensnikoff (1938) and in Berry v. Chaplin (1947) in both of which paternity was held to have been established despite the blood group evidence to the contrary.

In Jordan v. Mace (1949), however, the court took the view that evidence of blood grouping was more than merely expert opinion. Their view was that it was not open to the court to give such weight as it thought fit to what was a biological law. The function of the jury, they held, was limited to determining whether the conditions existed which made the biological law applicable and whether such tests had been properly carried out. In Ross v. Marx (1953) it was stated that "for a court to declare that these tests are not conclusive would be as unrealistic as it would be for a court to declare that the world is flat."

In our submission the more recent American approach to this problem represents the correct approach. The point to bear in mind is that evidence of blood grouping is not circumstantial evidence. It cannot be weighed in the scales against evidence as to whether the inquisitive neighbour did or did not see a tall dark man leaving the house in the small hours of the morning.

Either the evidence must be accepted as conclusive or treated as inadmissible. Once the courts have accepted the basis upon which such evidence is given then they must accept the evidence itself.

Consider the position of a toxicologist who gives evidence to the effect that he has carried out the Marsh test on the remains of the victim and has found five grains of arsenic which he states is a fatal dose. What can the jury do with such evidence? Unless conflicting evidence is presented to them they have no option but to accept it. Unless there is some other evidence for them to go on they cannot decide that the remains of the victim do not contain five grains of arsenic, nor can they decide that five grains is not a fatal dose.

The same is true, we would submit, in the case of blood group evidence. For a court to hold, in the face of contrary blood group evidence that the defendant is the father of a child is the same as deciding that the deceased did not die of arsenical poisoning in the face of unrefuted evidence to the contrary. No court would take this view in a poisoning case, and there seems no reason why they should do so in an affiliation suit. Providing that the evidence is such that the tests were properly performed by a properly qualified person then if the results are accepted at all they should be accepted as conclusive. The position was well summarised in the decision in Schulze v. Schulze (1942) in which the court pointed out that to reject the blood group evidence would be tantamount to holding either that the testimony of the physician was unworthy of credence, or that the tests themselves were futile. It is hardly open to courts today to argue on the basis of unreliability of the tests themselves - evidence of the results have been admitted in too many cases - so that the only valid ground for ignoring such evidence would be independent evidence relating to the abilities of the witness in performing the tests.

It is, of course, true that the position of blood group evidence, in most cases, is rather different from that of other forms of scientific evidence which the courts admit without showing any qualms. In most cases in which scientific evidence is tendered it is not tendered as disposing of the entire issue before the court. Thus, in the case of the toxicologist which we cited earlier, the evidence that he has found five grains of arsenic in the body, and his opinion that that is a fatal dose does not dispose of the issue before the court which is whether the prisoner was responsible for

the administration of the arsenic. In the case of blood group evidence, however, particularly in paternity cases, the evidence, if accepted, may dispose entirely of the issue. If the issue is whether the defendant is the father of a child, and the blood group evidence is to the effect that he could not be the father, then, if that evidence is accepted the whole issue before the court is decided.

The courts are doubtless justified in hesitating before abdicating their function to such an extent; hesitating, that is, until they are sure that the scientific claims are well founded. It would be our submission that those claims are now sufficiently well founded to justify a wide reception of such evidence.

An American Federal Court, in 1923, speaking of the use of evidence obtained by means of "lie-detectors" stated:

> 'Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognised, and while courts will go a long way in admitting expert testimony deduced from a well recognised scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field to which it belongs. We think the systolic blood pressure deception test has not yet gained such standing and scientific recognition among physiological and psychological authorities as would justify the courts in admitting expert testimony deduced from the discovery, development and experiments thus far made.'

We would submit that blood group evidence has now gained such standing and scientific recognition among physiological authorities as would justify the courts in admitting expert testimony deduced from the discovery, development and experiments thus far made, as conclusive of those matters to which it relates.

In thus arguing that the tests must be treated as conclusive we are not inconsistent with the points raised in the previous chapter in which it was admitted that the tests are not 100% accurate. The results do admittedly fall short of absolute accuracy, but if evidence of the results is to be admitted at all then that is a risk that must be faced and accepted on the basis that even if the results do fall short of perfection the accuracy obtainable is nevertheless very much greater than that obtainable by traditional methods.

It should finally be emphasised that the admission of the results of the tests as conclusive evidence is confirmed by those cases in which the results show an exclusion. It does not apply in those cases where the result shows that the defendant could have been the father or the source of a blood stain. Such evidence is purely circumstantial, and the court may attach such weight to it as it thinks fit.

POWER OF A COURT TO ORDER BLOOD TESTS

One problem which has frequently caused differences of opinion relates to the question whether, apart from statutory authority, a court has the power to order the parties or their witnesses to submit to blood tests. There appears to have been no discussion of this matter in either the English or Australian literature and it appears never to have been before their courts. The assumption seems to be that statutory authority is necessary for such an order. Without such an assumption a Bill to authorise such tests would hardly have been introduced into the House of Lords in England or a similar provision introduced into the New South Wales Act.

The problem, however, has been extensively considered in the United States and although many states have introduced legislation to authorise the courts making such orders, it should be borne in mind that in some jurisdictions the power to order blood tests is thought to be within the inherent power of a court at common law.

It is out submission that this latter view is the better view, that is to say that it is within the power of a common law court to order such tests, and that there are no reasons in either precedent or principle which prevent a court from so acting. In making this submission, however, we are fully aware that no English or Australian court is really likely to act in such a way. Except in American the common law seems to have passed its creative prime. This is the age of the legislature and the courts prefer to emphasise the need for legislation to deal with problems that arise rather than with dealing them themselves. As a matter of practical

reality, therefore, it must be admitted that if this problem is solved at all it will be solved by the passage of legislation. As a matter of academic interest, however, we indicate below the reasons on which we base our submission that the courts could, if they had the courage, order such tests.

The first point we would emphasise is that the courts have had, almost from the inception of the common law power to order medical examination of the parties. This power is exemplified in the old writ of de ventre inspiciendo under which the courts could order the inspection of a widow who claimed to be with child in order to guard the next heir against suppositititious births. Speaking of this writ Wigmore (1940) says:

> "the compulsory nature of this inspection was never doubted; and its firm place in our law is shown by the six centuries of time through which the employment of the writ persisted."

The earliest case in which the writ was ordered which we have been able to trace in the reports is Willoughby's case (1597). In subsequent cases, such as ex p. Aiscough (1731) ex p. Bellet (1786) and re Blakemore (1845) although the courts did much to ameliorate the rigors of the earlier procedure it was never doubted that in appropriate cases the examination was compulsory

Another example of compulsory medical examination under order of the court occurred in cases of mayhem. In these cases the court insisted on a medical examination in order to determine whether the injury was a main or a mere wound.

A third example is to be found in medical examinations which can be ordered in cases of nullity on the grounds of impotence. Instances of this type of examination, which can be traced back at least as far as the

Countess of Essex's case (1613), are to be found in W..... v. S..... (1905) and Intract v. Intract (1933). In W..... v. S..... the court pointed out that refusal by the wife to attend for such an examination would be taken as evidence against her, whilst in Intract v. Intract the court pointed out that the court had discretion in the matter of ordering such examinations and if satisfied that no useful purpose would be served by such an order may dispense with such an examination.

These cases establish the proposition that the court has power, at least in some circumstances, to order medical examination of the parties. It must be admitted, however, that in some circumstances such examinations have been denied. Thus on the basis that the wording of the relevant statute did not cover such a contingency the courts held, in re Betts (1888) that a bankrupt could not be compelled to undergo medical examination for life insurance purposes, and in Agnew v. Johson (1877) it was held, on a charge of concealment of birth, that a magistrate has no power to order medical examination of the female. Such cases, however, merely show that there are circumstances in which a court will not order medical examination, what they do not establish is that cases in which paternity is in question are cases in which the court should not order such examination.

That the power to order physical examinations exists can hardly be denied; the only question is whether the circumstances in paternity suits are such as to warrant the taking of blood tests, and all that can be said at the moment is that in neither England nor Australia has it yet been held that there is no justification for ordering such tests.

Consideration of the relevant American cases seems to reveal only two arguments against the power to order blood tests (apart that is from those which depend on the terms of the United States Constitution and which therefore have no relevance in either England or Australia.) The first of these is the rather extraordinary argument that to order such tests would be a serious assault and battery. This argument was actually sustained by the court in Commonwealth v. Krutsick (1946). An assault or battery is an illegal application of force, and what is lawfully ordered by a court can hardly be illegal. The question under discussion is whether a court has power to order such tests: if they have such power then the taking of the necessary blood samples cannot be an assault. Admittedly if they have not the power then to order such tests would be to require the commission of an assault, as in Agnew v. Jobson, quoted above, but the possible consequence of their not possessing the necessary power can hardly be used as an argument against their possessing the power.

A slightly different form of the same argument appeal to the "inviolability of the person". Such arguments are little more than an appeal to false rhetoric. Even if such a principle exists it is not absolute, for if it were it would be an argument against bodily examinations in the case of impotence for example. Assuming the principle, therefore, one must admit the existence of exceptions thereto, and the mere enunciation of the principle is no argument when considering whether, in any given case, an exception exists.

We turn, therefore, to consider the second argument used against the existence of an inherent power of a court to order blood tests. This is the argument that to order such tests would be to infringe the rule against self-crimination. This argument has been rejected in most American jurisdictions on the ground that the privilege against self-crimination only applies in the case of "testimony" and that in the case of blood group evidence, evidence as to the blood group of a party is not testimony which is supplied by him, and therefore outside the privilege. Wigmore (1940) puts the position as follows:

> "From the general principle it results that inspection of the bodily features by the tribunal or by witnesses cannot violate the privilege, because it does not call upon the accused as a witness i.e., upon his testimonial responsibility ..... What is obtained from the accused by such action is not testimony about his body, but his body itself. Unless some attempt is made to secure a communication, written or oral, upon which reliance is to be placed as involving his consciousness of the facts and of the operations of his mind in expressing it, the demand made upon him is not a testimonial one. Moreover the main object of the privilege is to force prosecuting officers to go out and search and obtain all the extrinsic available evidence of an offence without relying upon the accused's admissions. Now in the case of the person's body, its marks and traits, itself is the main evidence: there is ordinarily no other or better evidence available for the prosecutor. Hence the main reason for the privilege loses its force."

In an earlier passage Wigmore comments:

> "If an accused person were to refuse to be removed from the jail to the court-room for trial, claiming that he was privileged not to expose his features to the witnesses for identification, it is not difficult to conceive the judicial reception which would be given to such a claim."

This view was taken by the court in Davis v. State (1947), and, it is submitted, represents the correct approach to this problem.

It is on the arguments set out above that we base our submission that it is open to the English or Australian courts to order the parties in appropriate cases to submit to blood tests irrespective of particular statutory authorisation, ~~but~~ and simply relying upon their inherent powers of courts of justice. As long ago as 1877 in Schroeder v. C.R.I. & P. Ry. an American court emphasised the principle "if truth be hidden, injustice will be done" in the following terms:

> "We are often compelled to accept approximate justice as the best that the courts can do in the administration of law. But, where the law is satisfied with approximate justice where exact justice cannot be attained, the court should recognise no rules which stop at the first when the second is in reach."

and this principle should not be forgotten in considering the place of blood group testing today.

Finally we quote the almost savage words of Wigmore who, speaking of this very problem said:

> "How strange is this self-stultifying concession by a Court of Justice that it knows of no process to execute its powers for enforcing a condeded duty! Must there be a precise precedent for everything? Were the judges of Charles II or George III, who themselves were but the followers of six centuries of royal judges, the generation last vested with authority to apply old principles in new forms? Nobody has been able to find any definite authority for the 'duces tecum' form of subpoena; but the judges of 1808 were not moved by such trifling; such a power they declared is 'essential to the very existence and constitution of a Court of common law'. The mere phrasing of an auxiliary writ is not to stand in the way of inherent powers. Is there any known precedent of a writ to a court-bailiff ordering him to shut the doors to keep out an excessive throng, or to open the windows to let in fresh air? But no judge ever refrained from such orders because he had never seen such a form. The ordinary subpoena for a witness is of no avail when he is in prison: but the judges - somebody, sometime, no one knows who or when - varied the form of words and order the jailer 'habeas corpus ad testificandum'. They did not supinely sit and watch justice defrauded of testimony because the usual piece of parchment did not precisely fit the exigency. The Courts can as well command a witness to let the jury, or qualified experts, inspect his premises, his chattels, or his person, as to produce his documents. It is not to be supposed

that our Courts will finally commit themselves to the denial of such a plain dictate of principle and of commonsense."

Since the above was written the decision of the Court of Session in Whitehall v. Whitehall [1957] S.C. 252 has come to hand. Since this is the first United Kingdom case in which this issue has been directly raised it has been thought desirable to include some mention of it even at this late stage. The action was for divorce on the ground of adultery, the husband alleging that the child to which his wife had given birth was the offspring of adulterous intercourse. He expressed his willingness to submit to blood tests. The wife refused to agree to such a course so the husband then enrolled a motion requesting that the Court order the wife and her child to allow samples of their blood to be taken. The Lord Ordinary (Lord Wheatley) refused the motion. His Lordship's opinion is quoted in full below. He stated after setting out the facts:

> Pursuer's counsel admitted frankly that a motion of this nature was without precedent, but argued that since in cases of nullity and adultery a motion calling for inspection of the body of a party to the action had been approved the present motion should be likewise granted, because here the position was even more favourable to the pursuer, since the proposed examination involved nothing indelicate, indecent, or unbecoming such as might be involved in an inspectio corporis.
>
> The submission is indeed a novel one and before turning to examine the legal principles and the legal authorities which may bear upon the issue it is desirable to consider clearly what is involved in the proposal. The obvious purpose of the proposal is to ordain the defender to make available to the pursuer evidence which might be favourable to the pursuer's case and damaging to her own. If the blood tests disclosed that the pursuer was of the blood group consistent with him being the father of the child, it would go no further than establishing a negative fact, since it would not preclude the possibility of another man of the same blood group being the father. On the other hand if the result of the tests was such as to exclude the pursuer as being the father of the child by grouping, it would be strongly argued that such evidence was formidable and weighty if not altogether conclusive in support of the pursuer's case. In these circumstances the defender is being called

upon to provide to the pursuer the basis of evidence from which he has nothing to lose and a great deal to gain, while she has nothing to gain and a great deal to lose. A motion to ordain a party to a cause to provide to the other side a basis of evidence of such a nature is one to which I would not give effect unless I was obliged to do so by the authority of principle or precedent. It seems to me that the proposal offends against all conceptions of justice and is contrary to the fundamental principles of our law.

I accordingly turn to examine the cases quoted to me in support of the proposal to ascertain whether my instinctive view of the law is in any way controverted by precedents which are binding upon me, or by expressions of judicial opinion which, though not binding on me, might cause me to take an opposite view.

I was referred to passages in Walton, Husband and Wife, (3rd ed.) p. 8, and Fraser, Husband and Wife (2nd ed.) vol.i, p. 102, which were adduced in support of the proposition advanced by the pursuer's counsel. In the first instance these passages are referable to actions of nullity of marriage and, in my opinion, the considerations which apply in such a type of action would not necessarily cover an action of divorce on the ground of adultery. In the second place most of the statements in these textbooks are dependent on English authorities and I am not satisfied that in such cases the English procedure would necessarily commend itself to the Scottish Courts. In the two Scottish cases quoted in this field of law, both of which were Outer House decisions, the cases as reported do not seem to advance the pursuer's submission in this case to any extent. In the case of A.B. or D. v. C.D. (1908) 15 S.L.T. 911, the pursuer (a wife) sought decree of declarator of nullity of marriage on the ground of the impotency of the defender. The case was undefended and the defender at the time of the action was an inmate of a lunatic asylum. The pursuer moved the Court to appoint a medical inspection of the defender's person to take place and to appoint certain medical inspectors, maintaining that such an inspection was essential to her case. She did not, however, admit the defender's insanity. Lord Salvesen granted the motion. In doing so he said: "In England, for the law on this subject is substantially the same as our own, it seems to be the regular practice for the Court to order a medical inspection of the defender and if necessary this order will be enforced; although where the defender, being sane, refuses to submit to such an inspection, such refusal may in some cases be regarded as sufficient corroboration of the pursuer's evidence. As the defender is insane, I think, however, such an inspection should not take place unless with the permission of the asylum doctor." The facts that the action was undefended, that there was no opposition to the motion, and that the defender was insane may not be without a significant bearing on the decision which was reached in that case. Lord Salvesen, however, envisaged that the defender if sane might refuse to submit to such an inspection and expressed views with regard to the evidential effect of such a refusal on which I should like to reserve my own opinion. Be that as it may, I cannot regard that case as an authority in support of the proposition now advanced in a different form of action, and even if it were, since it is not binding on me, I would not be prepared to follow it in the present case.

The next case to be cited was that of X. v. X., 1922 S.L.T. 158. This was an action of adherence and aliment brought by a wife against her husband. In his defences the defender averred that the pursuer had persistently refused marital intercourse and that the marriage had never been consummated. The pursuer had submitted herself to examination by a lady doctor on her own behalf and a copy of that doctor's report was sent to the defender and his advisers. The defender thereafter moved the Court to ordain the pursuer to submit to a medical inspection by his doctor and despite opposition by the pursuer Lord Ashmore granted the motion. There is nothing in the report to indicate the grounds on which his Lordship proceeded, but it appears to me that a reasonable explanation of that decision can be found in the principle of fairness. The pursuer had indicated that she was prepared to lead medical evidence in connexion with an issue which formed an essential part of the case and in fairness it seemed but right that the defender should have an equal opportunity of presenting medical evidence on his behalf in respect of that issue, evidence which could only be obtained if the pursuer were to submit herself to a medical examination by a doctor on his behalf. In the present case, if the defender had obtained blood samples of herself, the child and the pursuer and had intimated to him that she intended using the results of these tests in support of her case, then the argument of fairness might well have been invoked to support a motion such as is now before the Court in order to give the pursuer an opportunity of adducing counter-evidence on that issue. That, however, is far from being the case here and accordingly I cannot see that the decision in X. v. X., which seems to me to be based on such a speciality, provides any support for the pursuer's contention. Support for the view which I have taken on the touchstone of fairness seems to me to be derived from the judgment of the Judges of the First Division in the case of Davidson v. Davidson (1860) 22 D.749. In that case the wife raised an action for divorce against her husband alleging that he had had sexual intercourse with A, who, in her deposition as a witness, denied that allegation and stated that her person had been inspected by an eminent medical man. There was in process evidence corroboratory of her denial. The medical man who had examined her was tendered as a witness with a view to proving A was virgo intacta. On the ground that the Court had no power to order such an examination and that the evidence must be confined to that of medical men selected by the party alone, the evidence was rejected. The procedure which was at that time followed in cases of this nature differs substantially from the present procedure. None the less their Lordships of the First Division came to the conclusion that the proposed course was objectionable on two grounds which I may paraphrase as follows:- (1) the person sought to be medically examined was not a party to the case, and (2) where one side had obtained an advantage in evidence through the consent of the witness and there was no authority in the Court to compel such a witness to grant a like advantage to the other side, it was only right that the principle of fairness should regulate the decision. In Davidson that principle was operated by excluding the evidence altogether.

In the present case the defender is not seeking to obtain any advantage which could not be enjoyed by the pursuer and in these circumstances I do not consider that she in turn should be called upon to provide an advantage to the pursuer which she herself cannot enjoy. The case, however, was prayed in aid for passages in the opinions of Lord Curriehill and Lord Deas which were said to be apposite to the present case. Lord Curriehill said: "There may be another class of cases as to which I give no opinion. Where the evidence is necessary and indispensable to the ends of justice, I say nothing as to its admissibility." Lord Deas stated: "Now, though I am not disposed to say there may not be circumstances in which an inspection of this kind may be competent, I think it would require great consideration how it was to be done." Both of these expressions of opinion are of course obiter dicta and they certainly do not indicate in conclusive terms the conditions under which their Lordships thought that an inspection might be competently ordered. I certainly do not consider that such circumstances arise in the present case, and I see nothing in the judgments in the case of Davidson which provide authority for an otherwise unprecedented and in my view unsupported proposition. On the contrary, however, in so far as the motion includes an order on the defender to make available a sample of blood of the child Elaine, who is not a party to the action, the decision in Davidson seems an authority in support of the motion being refused. The making available of a sample of Elaine's blood might not only have the effect at the end of the day of leading the Court to an inference of adultery on the part of the defender, but might also establish in due course the bastardy of Elaine herself. In these circumstances it seems to me that on any view of the law that part of the motion must be refused. Without a sample of Elaine's blood it would of course be useless to submit to tests samples of blood from the pursuer and the defender, and that fortifies the conclusion which I have otherwise reached in respect of the motion as a whole.

In the whole circumstances, therefore, I have come to the conclusion that the motion should be refused.

It will be noted that his Lordship's argument follows the well worn lines indicated in the discussion of this problem above. His Lordship's main point seems to have been that blood test evidence might be effective:

> The making available of a sample of Elaine's blood might not only have the effect at the end of the day of leading the Court to an inference of adultery on the part of the defender, but might also establish in due course the bastardy of Elaine herself.

If evidence is to be excluded on the ground that it is relevant to the point at issue the Courts have really reached an extraordinary position, and equally if one party to an action can refuse to make evidence available simply on the ground that it tends to support the other side (the case not coming within one of the established exceptions, such as evidence tending to criminate) litigation will become a more hazardous affair than it is even now.

It should be further added that Lord Wheatley's opinion was upheld on appeal before the Second Division although unfortunately the terms of the decision were not available to us by the time that this dissertation had to be handed over to the authorities.

The only comment that seems to be necessary is that the decision supports our prediction that legislation will be necessary to introduce compulsory blood testing in the United Kingdom.

CONCLUSION

We have far from exhausted all the aspects of blood group testing in the foregoing pages, but it is hoped that sufficient of the background has been given to render the major medico-legal applications of blood groups explicable. One thing at least is clear, namely, that as serology continues to advance the current applications will become more and more detailed and more and more accurate whilst yet further applications will be discovered.

APPENDIX I

[2 & 3 GEO.6.] BASTARDY (BLOOD TESTS). [H.L.]

A

BILL

[As Amended by the Select Committee]

INTITULED

An Act to empower Courts of Summary Jurisdiction and Courts hearing appeals therefrom to require an applicant for an affiliation order, her child and the defendant to undergo blood tests; and for purposes connected therewith.

BE it enacted by the King's most Excellent Majesty, by and with the advice and consent of the Lords Spiritual and Temporal, and Commons, in this present Parliament assembled, and by the authority of the same, as follows:-

1. - (1) Upon the hearing of an application for an affiliation order under the Bastardy Laws Amendment Act, 1872, or under any Act amending the same, the Court may and at the request of the defendant shall by order require the applicant, her child and the defendant to undergo blood tests to ascertain whether such tests show that the defendant is thereby excluded from being the father of the child, and if the applicant refuses the Court shall dismiss the application.
(2) Nothing in this section shall affect the power of the Court to adjourn the hearing of the application from time to time.

2. - (1) If the applicant consents, the Court shall nominate an approved person to carry out tests on the blood of the applicant, of her child and of the defendant in accordance with rules made under this Act.
(2) Blood tests shall be carried out only by the approved person nominated by the Court, at an approved testing centre.
(3) For this purpose, blood samples of the applicant, of her child and of the defendant shall be taken by a registered medical practitioner, who shall where practicable be the applicant's regular medical attendant.

3. - (1) An approved person who has carried out blood tests shall, as soon as may be practicable, send to the clerk of the Court a certificate specifying the results of the tests in the form set forth in rules made under this Act.
(2) The clerk of the Court shall, not more than seven days after receiving it, send a copy of the certificate to the applicant and to the defendant.

(3) The certificate shall be produced to the Court by the clerk and shall be sufficient evidence of the facts and conclusions stated therein, unless the Court or either party require that the approved person by whom the certificate is signed shall be called as a witness.
(4) If the certificate does not show that the defendant is excluded from being the father of the child -

(i) the certificate shall not be made the subject of comment to the Court by or on behalf of either party;
(ii) the certificate shall not be admissible as evidence corroborating the evidence of the applicant.

4. - (1) The Court may by order direct the payment of the whole or any part of the costs of carrying out the tests and giving their results in evidence out of the local funds.
(2) The Court may order either party to pay the whole or such part of the costs thereof as it thinks fit.
(3) If an approved person who has signed a certificate attends as a witness at the request of either party the Court may order that party to pay the whole or such part of the costs of his attendance as it thinks fit.
(4) The Court may require a party ordered to pay costs as aforesaid to give security for the whole or any part thereof in the manner provided by section 23 of the Summary Jurisdiction Act, 1879.

5. - (1) This Act is an enactment relating to bastardy within the meaning of subsection (2) of section thirty-seven of the Criminal Justice Administration Act, 1914.
(2) A court of Quarter Sessions hearing an appeal from any decision of a court of summary jurisdiction under the enactments relating to bastardy shall have power to make any order which a Court may make under this Act upon the hearing of an application for an affiliation order, including power to order blood tests to be carried out, whether a blood test has already been carried out or not.

6. - (1) The Lord Chancellor may make rules under this Act governing -

(a) the procedure and functions of the blood tests board;
(b) the selection of approved persons and of approved testing centres;
(c) the duties of approved persons and the conduct of approved testing centres;
(d) the taking, identification and transport of blood samples and the conduct thereon of blood tests;
(e) the certification to the Court of the results of blood tests;
(f) the fees and expenses payable to approved persons and medical practitioners;
(g) all other matters necessary to the effective administration of this Act.

(2) Any rules made under this Act shall be laid before Parliament as soon as may be after they are made, and if either House of Parliament, within the next period of forty days beginning with the date on which the rules are laid before it, resolves that the rules be annulled, the rules shall thereupon become void, without prejudice, however, to the validity of anything previously done thereunder or to the making of new rules.

In reckoning any such period of forty days as aforesaid no account shall be taken of any time during which Parliament is dissolved or prorogued or during which both Houses are adjourned for more than four days.

7. - (1) For the purpose of making rules under this Act and of giving advice and assistance to the Lord Chancellor in the administration of the Act and of the rules, a Blood Tests Board (hereinafter referred to as "the Board") shall be appointed.

(2) The Board shall consist of ten members of whom one member shall be nominated by each of the following:-

The Lord Chancellor,
The General Council of the Bar,
The Law Society,
The Magistrates' Association,
The Incorporated Justices' Clerks' Society,
The Royal College of Physicians of London,
The Royal College of Surgeons of England,
The Royal College of Obstetricians and Gynaecologists,
The Medical Research Council,
The British Medical Association.

(3) Subject to the provisions of this Act and to the rules, the Board may make regulations governing their procedure and may at their discretion consider and report to the Lord Chancellor upon any matters affecting the administration of this Act and of the rules.

8. - (1) If any person contravenes the provisions of any rule made under this Act, he shall be liable on summary conviction to a fine not exceeding five pounds, or, if he commits a second or subsequent offence, not exceeding twenty pounds.

(2) If any person wilfully and fraudulently personates any party whom the Court has ordered to undergo blood tests, or wilfully or fraudulently proffers for test a child other than the child named in the order, or makes a declaration in accordance with the rules made under this Act which is false in a material particular, he shall be liable to a fine not exceeding twenty pounds or to imprisonment not exceeding six months or both.

9. In this Act -

the expression "blood tests" shall mean blood tests carried out under this Act and under the rules and shall include any test made with the object of ascertaining the inheritable characteristics of blood;

the expression "approved person" shall mean a registered medical practitioner, who is also a pathologist, approved by the Lord Chancellor on the recommendation of the Board as competent to carry out blood tests under this Act;

the expression "blood samples" shall mean blood taken from a person for the purpose of blood tests;

the expression "approved testing centre" shall mean a place approved by the Lord Chancellor on the recommendation of the Board as fit for the conduct of blood tests; and

the expression "local funds" shall mean the funds of administrative counties or county boroughs as defined in section four of the Costs of Criminal Cases Act, 1908.

10. This Act shall not apply to Scotland or to Northern Ireland.

11. This Act may be cited as the Bastardy (Blood Tests) Act, 194 , and shall come into operation on the first day of January nineteen hundred and forty

APPENDIX II

UNIFORM ACT ON BLOOD TESTS TO DETERMINE PATERNITY

9 Uniform Laws Ann.19

§ 1. Authority for Test. In a civil action, in which paternity is a relevant fact, the court, upon its own initiative or upon suggestions made by or on behalf of any person whose blood is involved may, or upon the motion of any party to the action made at a time so as not to delay the proceedings unduly, shall order the mother, child and alleged father to submit to blood tests. If any party refuses to submit to such tests, the court may resolve the question of paternity against such party or enforce its order if the rights of others and the interests of justice so require.

§ 2. Selection of Experts. The tests shall be made by experts qualified as examiners of blood types who shall be appointed by the court. The experts shall be called by the court as witnesses to testify to their findings and shall be subject to cross-examination by the parties. Any party or person at whose suggestion the tests have been ordered may demand that other experts, qualified as examiners of blood types, perform independent tests under order of court, the results of which may be offered in evidence. The number and qualifications of such experts shall be determined by the court.

§ 3. Compensation of Expert Witnesses. The compensation of each expert witness appointed by the court shall be fixed at a reasonable amount. It shall be paid as the court shall order. The court may order that it be paid by the parties in such proportions and at such times as it shall prescribe, or that the proportion of any party be paid by (insert name of the proper public authority) and that, after payment by the parties or (insert name of the public authority) or both, all or part or none of it be taxed as costs in the action. The fee of an expert witness called by a party but not appointed by the court shall be paid by the party calling him but shall not be taxed as costs in the action.

§ 4. Effect of Test Results. If the court finds that the conclusions of all the experts, as disclosed by the evidence based upon the tests, are that the alleged father is not the father of the child, the question of paternity shall be resolved accordingly. If the experts disagree in their findings or conclusions, the question shall be submitted upon all the evidence. If the experts conclude that the blood tests show the possibility of the alleged father's paternity, admission of this evidence is within the discretion of the court, depending upon the infrequendy of the blood type.

§ 5. Effect of Presumption of Legitimacy. The presumption of legitimacy of a child born during wedlock is overcome if the court finds that the conclusions of all the experts, as disclosed by the evidence based upon the tests, show that the husband is not the father of the child.

§ 6. Applicability to Criminal Actions. This act shall apply to criminal cases subject to the following limitations and provisions:

(a) an order for the tests shall be made only upon application of a party or on the court's initiative;

(b) the compensation of the experts shall be paid by (insert name of proper public authority) under order of court;

(c) the court may direct a verdict of acquittal upon the conclusions of all the experts under the provisions of section 4, otherwise the case shall be submitted for determination upon all the evidence.

§ 7. Uniformity of Interpretations. This act shall be so interpreted and construed as to effectuate its general purpose to make uniform the law of those states which enact it.

§ 8. Severability Clause. If any part of this act is declared invalid the remaining portion shall continue in full force and effect and shall be construed as being the entire act.

§ 9. Short Title. This act may be cited as the Uniform Act on Blood Tests to Determine Paternity.

§ 10. Repeal. All acts or parts of acts which are inconsistent with the provisions of this act are hereby repealed.

§ 11. Time of Taking Effect. This act shall take effect . . . . . .

APPENDIX III

Uniform Act on Blood Tests (as amended by the A.M.A.)

Be it enacted.....

1. In a civil action in which parentage is a relevant fact, the court, upon its own initiative or upon motion of any party in the action shall order the mother, child and alleged father, to submit to blood tests.

2. The test shall be made by qualified experts in the field of blood grouping who shall be appointed by the court. For a list of such experts the court shall apply to the local medical association or to the American Medical Association. The expert may be called by the court to testify on the findings and shall be subject to cross examination. Any party may demand that other qualified experts perform independent tests under order of the court.

3. The compensation of each expert appointed by the court shall be fixed at a reasonable amount, and paid as the court shall order.

4. If the blood tests show that the alleged parent is not the parent of the child, such a finding shall be admissible as evidence. If the blood tests show the possibility of the alleged parent's parentage, the admission of such evidence shall be within the discretion of the court.

5. The presumption of the legitimacy of a child born during wedlock is overcome if the court finds that the blood tests show that the husband is not the father of the child.

6. This act shall also be applicable in criminal cases in which the problem of parentage arises, such as cases of rape and kidnapping.

7. If any part of this act is declared invalid the remaining portion shall continue in full force and effect and shall be construed as being the entire act.

8. This act may be cited as the Uniform Act for Blood Tests in Disputed Parentage in Man.

9. (Repeal)

10. (Time of taking effect)

APPENDIX A

Child Welfare Act (No. 17,1939)

New South Wales

S. 120 (1) This section shall commence upon a day to be appointed by the Governor and notified by proclamation published in The Gazette.

(2) In this section "blood test" means a test made for the purpose of ascertaining the inheritable characteristics of blood.

(3) (a) A children's court consisting of a special magistrate shall, at the request of any person against whom an order for the expenses of maintenance which has been made or is deemed to have been made under this Part is in force or of the parties to any proceedings or contemplated proceedings under this Part, direct that the child in respect of whose maintenance the order was made or the proceedings are taken or contemplated, the mother of the child and the man adjudged or alleged to be the father of the child submit to blood tests. No such direction shall be given unless the child has been born and the child, its mother and the man concerned are all living.

(b) When any such direction is given the magistrate shall in obeying the direction nominate a medical practitioner to take such blood sample as may be necessary for the purpose of making the blood test and a pathologist to make the blood test and shall also fix a period within which the child, the mother and the man concerned shall attend such medical practitioner for the purpose of the taking of such sample.

Any period so fixed may be extended from time to time as the magistrate may think fit.

The pathologist so nominated shall be a medical practitioner whose name is on a panel of names of medical practitioners authorised to carry out blood tests under this Part, which panel shall be prepared by the Minister on the recommendation of the Director-General of Public Health.

(4) When a direction has been given by a magistrate under subsection three of this section the following provisions shall have effect:-

(a) When the hearing of a complaint under subsection one of section ninety-nine of this Act is pending

(i) proceedings in such hearing shall be stayed until the expiration of the period or extended period fixed under subsection three of this section;

(ii) if the mother and the child referred to in the direction or either of them does not within such period or extended

period attend the medical practitioner nominated in the direction and permit him to take blood samples, the complaint shall be dismissed and a further complaint shall not be allowed under section one hundred and thirteen of this Act unless the mother gives an undertaking to submit herself and the child to blood tests;

(iii) if the defendant to such complaint does not within such period or extended period attend the medical practitioner nominated in the direction and permit him to take blood samples the complaint shall be set down for hearing.

(b) Where an order for expenses of maintenance made or deemed to be have been made under this Part is in force -

(i) if the mother and the child referred to in the direction or either of them do not, within such period or extended period, attend the medical practitioner nominated in the direction and permit him to take blood samples, the order shall, as from the expiration of such period or extended period, be suspended until the direction is complied with by the mother and the child, and if the direction is not complied with within a reasonable time, the order may be discharged;

(ii) if the person liable under the terms of the order to pay the expenses of maintenance does not, within such period or extended period, attend the medical practitioner nominated in the direction and permit him to take blood samples the direction under subsection three of this section shall lapse.

(c) The special magistrate may adjourn the proceedings from time to time as such special magistrate shall think fit.

(d) The fee of the medical practitioner nominated in the direction and the costs and expenses payable in connection with the making of the blood test shall be paid by the person at whose request the direction was given.

(5) The medical practitioner nominated in a direction given under subsection three of this section shall in the manner and within the time prescribed forward all blood samples taken by him pursuant to the direction to the pathologist nominated in the direction. The blood test shall be made by the pathologist nominated in the direction, and the results of such test shall be embodied in a certificate in the prescribed form.

(6) The certificate given under subsection five of this section shall be forwarded

(a) in any case where the direction was given by the Metropolitan Children's Court or by a magistrate exercising jurisdiction within the area named in the proclamation establishing the

Metropolitan Children's Court - to the Clerk of the Metropolitan Children's Court.

(b) in any other case - to the Clerk of Petty Sessions for the district within which the magistrate giving the direction exercises jurisdiction.

The Clerk of the Metropolitan Children's Court or the Clerk of Petty Sessions, as the case may be, shall, within seven days of the receipt by him of the certificate, send a copy of the certificate to the parties concerned.

(7) A certificate given under subsection Five of this section shall be admissible as evidence in any proceedings under this Part, and shall be evidence of the facts and conclusions stated therein.

(8) The regulations may prescribe all matters necessary or convenient to be prescribed for carrying out or giving effect to this section.

Without prejudice to the generality of the foregoing provision the regulations may prescribe

(a) the duties of medical practitioners nominated to take blood samples, in relation to such samples;

(b) the scale of fees to be paid to medical practitioners so nominated;

(c) the scale of costs and expenses payable in connection with the making of the blood test.